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THE DISTENTION FACTOR IN SIMPLE INTESTINAL OBSTRUCTION

AN EXPERIMENTAL STUDY WITH EXCLUSION OF SWALLOWED AIR BY CERVICAL ESOPHAGOSTOMY

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IT HAS become increasingly apparent that the factor of distention plays a significant role in the sequence of events which attends obstruction of the bowel. Up until about fifteen years ago, it was believed largely that absorption of abnormal toxins formed during the course of the obstruction was the important determinant which brought about a lethal issue. The breakdown of this hypothesis began with an understanding of the effects of dehydration and dechlorination which accompanied pyloric and duodenal obstruction or fistula.[2, 3] The demonstration of the efficacy of saline solution in prolonging the lives of dogs with duodenal obstruction served to make the significant lethal factor in high intestinal obstructions fairly well understood.[4, 6]

The cause of death in experimental ileal obstructions has defied complete understanding and has been the subject of considerable conjecture.[9] The administration of saline solution fails to prolong life materially in experimental ileal obstructions in dogs; whereas, obstruction of the pelvic colon in the dog may be survived for long periods of time without the administration of saline solution. Attempts have been made repeatedly in this laboratory to elucidate the mechanism of the lethal factor in experimental ileal obstructions.[1, 16, 17] It

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has been our belief that inability to empty the lower reaches of the gut by vomiting causes it to become distended with ensuant sustained increments of intraluminal pressure attended in turn by interference with blood flow and satisfactory oxygenation. By severing the terminal ileum and anastomosing the proximal end to the stomach (end-to-side), it was found possible to keep a dog alive for fifty-six days (Fig. 1). In this animal the ileal content was returned to the stomach, from which vantage level it was the more readily evacuated by vomiting.[17]

Demonstration of the possibility of relieving certain mechanical intestinal obstructions by suction applied to an inlying duodenal tube lent credence to the belief that distention with its associated sequelae was the item of chief importance in causing death in ileal obstruction.

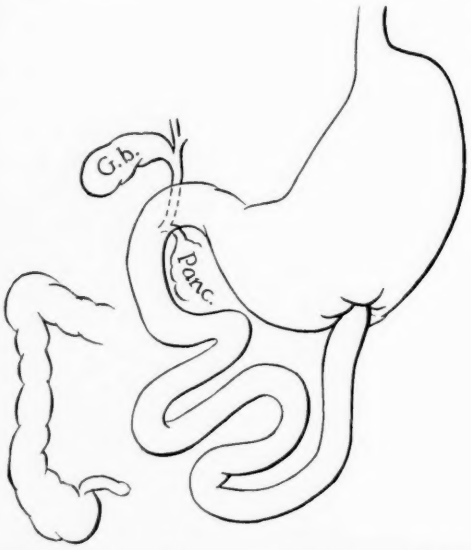

Fig. 1.—Dogs survive complete obstruction of the terminal ileum for 7 to 8 days. When saline solution is given subcutaneously, dogs survive 8 to 10 days; an occasional dog survives somewhat longer. Anastomosis of the terminal ileum to the stomach permits dogs to survive much longer (one animal survived 56 days). This operation obviates sustained increase of intraluminal pressure in the terminal ileum. A preliminary ileosigmoidostomy[11] before the establishment of ileal obstruction increases also the survival period. (Reproduced here from Wangensteen, O. H., and Leven, N. L.: Arch. Surg. 22: 658, 1931.)

The agents which cause distention are gas and the digestive juices. McIver and his associates[8] have shown swallowed air to be the principal source of gaseous distention of the stomach after abdominal operations. In this laboratory it has been shown that swallowed air accounts for about 68 per cent of the gas present in instances of simple mechanical obstruction.[7]

Having in mind the great absorptive capacity of the small intestine, it is quite reasonable to assume that, if swallowed air could be excluded from the intestine even in the presence of obstruction, the

digestive juices could be absorbed and obstruction of the terminal ileum be tolerated fairly well. It was with this premise in mind that we began in May, 1933, to study the effects of ileal obstruction in the dog with exclusion of swallowed air from the intestine by cervical esophagostomy.

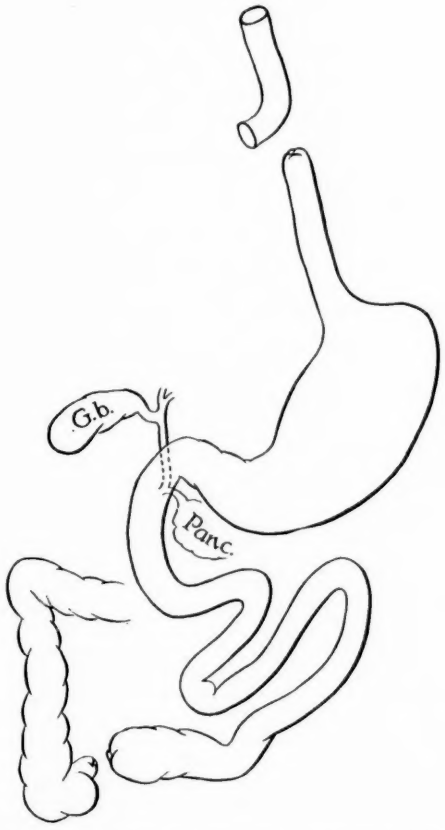

Fig. 2.—Cervical esophagostomy to exclude swallowed air. Complete ileal obstruction is tolerated well under these conditions and dogs survive for long periods when saline solution is given liberally subcutaneously. The gut is usually not distended at autopsy. The cause of death is starvation. It is necessary, however, to invert the distal end of the cervical esophagus, for if it is not occluded, the animals still swallow considerable quantities of air.

METHODS

A cervical esophagostomy was established in dogs by a two-stage operative procedure (intraperitoneal pentobarbital anesthesia, 35 mg. per kilogram of body weight) in which the esophagus was first isolated and elevated, a slip of the left sternocleidomastoid muscle being drawn beneath it. When the wound was well healed (usually in about a week), the esophagus was transected and both ends were brought out to the skin. For varying periods of time, lengthened as the investigation proceeded from one to two to four weeks, the dog was maintained by liberal feedings of the Scott-Ivy pabulum[10] administered by

catheter into the distal opening of the cervical esophagus. The weight loss of the dogs in the latter experiments in which esophageal feeding was maintained for four weeks after the establishment of the esophageal fistula was uniformly less than 10 per cent of the initial weight. Then, following a period of starvation of twenty-four hours, the terminal ileum was obstructed by dividing the gut and inverting both ends. On completion of the procedure, the distal end of the transected esophagus was inverted carefully. In the earlier experiments the distal end of the esophagus was left open, but it was learned quickly that such an animal swallowed as much air as a dog with the esophagus intact. The dogs were then maintained up until death by the daily subcutaneous administration of physiologic saline solution. In the earlier experiments 600 c.c. of saline solution was given once daily. In the latter experiments 1,500 c.c. was given daily in two divided doses. A few of the last dogs operated upon were transfused a few times with blood from other dogs in an attempt to increase the values for the plasma proteins which became lowered considerably by the prolonged period of starvation. To the final dog in the series, whose survival period was longest (Table III, Dog 11), the vitamins B_1(1 mg.) and C(100 mg.) were given subcutaneously each day during the last three weeks of life. In addition, an intramuscular injection of 20 c.c. of a 10 per cent solution of glycine was given daily, and also daily retention enemas of 100 c.c. of 5 per cent aqueous dextrose solution and one ounce of cod-liver oil, which, however, were retained poorly. When it became apparent that the animal was moribund, he was killed with an intracardiac injection of ether. At the time of autopsy, the absence or presence of distention was noted and the amount of gas and fluid present was determined.

Control survival periods were determined for dogs with esophagostomy and for animals with obstruction of the terminal ileum given saline solution subcutaneously (Table I). Animals which developed infection in the cervical wounds were excluded in this consideration.

RESULTS

The early results which have been briefly reported elsewhere[15] were disappointing. For, despite the finding of a gut which was usually collapsed save for a short segment immediately proximal to the obstruction, the survival period for the dogs with ileal obstruction upon which esophagostomy for the exclusion of swallowed air had been performed was found to be no longer than in the controls in which obstruction of the terminal ileum alone had been done and in which animals distention was a prominent feature. These early results in

TABLE I

CONTROLS

OPERATION	DOG (NO.)	INITIAL WEIGHT (KG.)	SALINE SOLUTION (C.C.)	SURVIVAL (DAYS)			GAS (C.C.)			FLUID (C.C.)			WEIGHT AT DEATH (KG.)
A. Esophagostomy	28	12	0	7			Gut collapsed			Gut collapsed			9.6
	29	12	0	6			Gut collapsed			Gut collapsed			9.0
	30	10	0	6			Gut collapsed			Gut collapsed			4.0
	31	10	0	8			Gut collapsed			Gut collapsed			7.5
	14	7	0	4			Gut collapsed			Gut collapsed			5.0
	75	10	0	4			Gut collapsed			Gut collapsed			8.2
	No. dogs			Avg.	Min.	Max.	Avg.	Min.	Max.	Avg.	Min.	Max.	% loss
Average	6			6	4	8	Almost none			Almost none			25
B. Esophagostomy*	103	12	600	23			Almost none			Almost none			7.2
	104	12	600	22			Almost none			Almost none			8.0
	105	16	600	10			Almost none			Almost none			10.0
	No. dogs			Avg.	Min.	Max.	Avg.	Min.	Max.	Avg.	Min.	Max.	% loss
Average	3			18	10	23	Almost none			Almost none			40
C. Terminal ileal obstruction	2	15	0	3			300			200			12.5
	3	15	0	7			250			150			12.0
	15	18	0	8			700			400			15.0
	17	10	0	10			200			100			8.0
	18	13	0	8			300			150			10.5
	19	10	0	12			350			200			8.0
	No. dogs			Avg.	Min.	Max.	Avg.	Min.	Max.	Avg.	Min.	Max.	% loss
Average	6			8	3	12	350	200	700	200	100	400	16
D. Terminal ileal obstruction + saline solution	6	10	600	7			400			300			9.2
	7	12.5	600	5			300			200			11.5
	12	14	600	8			350			400			13.0
	13	15	600	8			250			250			14.0
	24	9.5	600	7			200			100			8.5
	No. dogs			Avg.	Min.	Max.	Avg.	Min.	Max.	Avg.	Min.	Max.	% loss
Average	5			7	5	8	300	200	400	250	100	400	7

*The average survival period of three other dogs with esophagostomies given 1,000 c.c. of saline solution subcutaneously every day was 43 days.

which no direct correlation was obtained between the length of survival and the presence or absence of distention in the gut at necropsy left us somewhat confused with reference to the significance of the distention factor. However, in the light of the success which was attending conservative decompression of the obstructed bowel in man by suction applied to an indwelling duodenal tube, we were not ready to conclude that a "toxic factor" was responsible.

Fig. 3.—Photograph of the condition found at autopsy in Dog 11 (Table III). This animal survived complete ileal obstruction with cervical esophagostomy for 57 days. The terminal reaches of the gut are slightly distended. The entire closed loop of esophagus, stomach, and entire small intestine contained 125 c.c. of fluid and 100 c.c. of gas.

The earlier experiments were performed during the course of a very hot summer (1933). With gradual lengthening of the time between performance of esophageal fistula and establishment of obstruction in the terminal ileum (four weeks), with the more liberal administration of saline solution (1,500 c.c. of one per cent daily), avoidance of experimentation during the hot summer months, occasional transfusion of blood toward the end of the experiment, and use of only large and older dogs, it became apparent that when swallowed air was excluded from the bowel the obstructed gut could resorb effectually the digestive juices from the bowel. The cause of death in the animals with

long survival periods, which were obtained fairly uniformly in the latter experiments, would appear to have been starvation.

From an inspection of the tables, it is to be noted that esophagostomy diminishes notably the amount of gas and fluid found at necropsy as contrasted with the animals having ileal obstruction but no exclusion of swallowed air (compare Table I *C* and *D* with Table II *A* and *B*

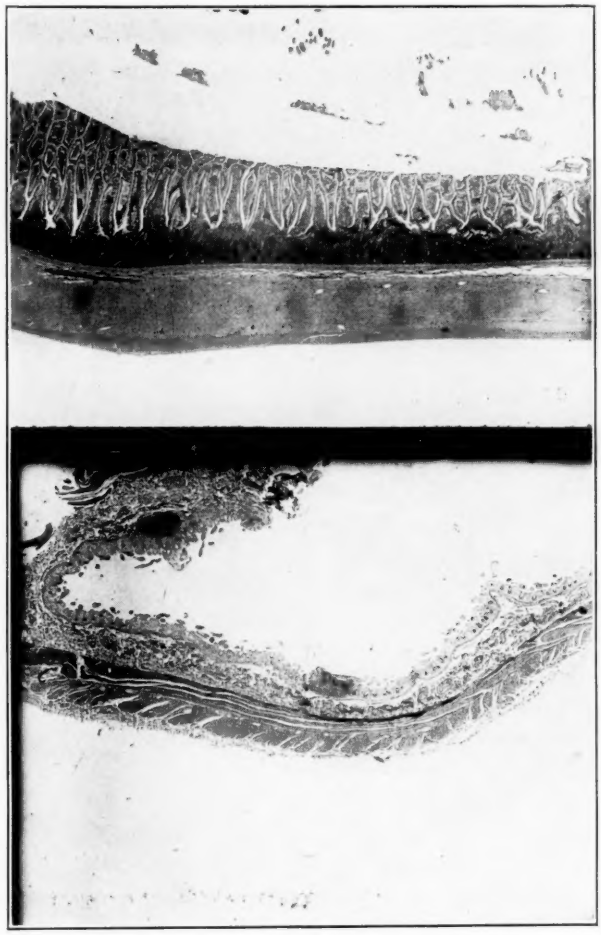

Fig. 4.—*A*, Photomicrograph (×12½) indicating the hypertrophy of the muscle of the gut wall (near obstruction) as contrasted with *B*, the normal terminal ileum at a comparable level.

and Table III). In a few of the animals with long survivals (Table III) in which esophagostomy had been performed, a surprisingly large amount of fluid or gas and fluid was found in the obstructed bowel at necropsy. In two of these (Dogs 9 and 10) reasonable causes operated to bring the condition about. In Dog 9 a volvulus was brought about by rotation of the obstructed gut about an adhesive band; in the other, food had been present in the stomach at the time of opera-

TABLE II

ESOPHAGOSTOMY + OBSTRUCTION

OPERATION	DOG	INITIAL WEIGHT (KG.)	SALINE SOLUTION (C.C.)	SURVIVAL (DAYS)	GAS (C.C.)	FLUID (C.C.)	WEIGHT AT DEATH (KG.)
A. Esophagostomy + terminal ileal obstruction	8	8.2	0	2	75	25	6.8
	9	10.4	0	2	100	180	8.5
	11	7.3	0	4	60	100	5.5
	20	13.0	0	4	65	40	11.6
	21	10.0	0	4	50	15	6.2
	22	9.5	0	2	40	20	7.5
	25	10.0	0	3	60	150	5.5
	26	11.5	0	2	30	40	8.0
	49	15.0	0	3	50	50	13.0
	73	13.5	0	4	100	50	11.6
Average	No. dogs 10			Avg. 3 Min. 2 Max. 4	Avg. 53 Min. 30 Max. 120	Avg. 67 Min. 15 Max. 150	
B. Esophagostomy + terminal ileal obstruction + saline	76	10.0	600	5	75	80	9.5
	77	12.5	600	4	85	100	10.0
	78	9.4	600	5	10	60	8.2
	90	12.5	600	6	120	100	10.0
	91	10.0	600	3	30	100	7.2
	92	10.0	600	5	210	80	7.0
	93	13.0	600	11	60	200	10.5
	94	14.5	600	5	100	630	11.5
	95	10.0	600	3	100	150	6.8
	96	12.5	600	5	35	210	10.0
	80	15.0	600	5	100	140	13.0
	81	10.0	600	4	80	200	8.5
	82	10.0	600	6	180	110	8.5
	102	11.5	600	19	60	200	8.5
	106	10.0	600	16	40	140	7.0
	107	15.0	600	20	85	200	11.5

TABLE III

ESOPHAGOSTOMY AND OBSTRUCTION

OPERATION	DOG (NO.)	INITIAL WEIGHT (KG.)	SALINE SOLUTION (C.C.)	SURVIVAL IN DAYS	GAS (C.C.)	FLUID (C.C.)	WEIGHT AT DEATH (KG.)	REMARKS
Esophagostomy + feeding for 1 month; then closure of the distal esophageal opening and terminal ileal obstruction + saline solution	1	24.0	1,500	19	100	150	16.5	Dogs 1-7 showed no distention of the gut except for segment 15 to 20 cm. proximal to ileal obstruction
	2	20.0	1,500	20	150	50	16.0	
	3	17.5	1,500	32	0*	100	12.0	
	4	26.0	1,500	40	50	50	15.2	Dog 4 received 2 transfusions of citrated blood, 300 c.c. each.
	5	15.9	1,500	29	0*	350	12.5	
	6	17.0	1,500	45	50	60	11.5	Total plasma protein just before death, 4.5 gm. %
	7	18.5	1,500	34	0*	90	10.0	
	8	18.0	1,500	33	175	150	13.5	Slight distention
	9	15.0	1,500	33	600	800	9.5	Died with a volvulus; gut markedly distended
	10	20.0	1,500	45	1,000	350	14.5	Stomach and jejunum are contracted; received 4 transfusions of citrated blood, 300 c.c. each, after ileal obstruction
	11	18.3	1,500	57	100	125	12.5	Ileum was distended and contained 500 gm. of semisolid fecal material; this dog received a total of 5 transfusions of citrated blood, 300 c.c. each, after the ileal obstruction; just before the animal was sacrificed, plasma protein 4.4 gm. %, plasma chlorides 676 mg. %, and nonprotein nitrogen 60.6 mg. %

*Too small to be accurately measured.

tion. In a previous study the nature of the gas found in the obstructed bowel, which was essentially a closed loop, was reported earlier. Seventy-five per cent of the gas was nitrogen, an indication that the more diffusible gases originating within the closed loop had been displaced largely by diffusion of nitrogen into the bowel lumen from the blood stream.[7]

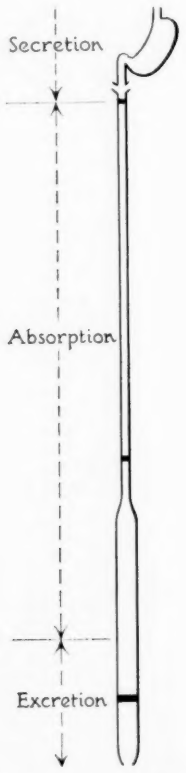

Fig. 5.—The intestine projected as a straight tube. The effects of obstruction at various levels are discussed in the text. (Reproduced here from Wangensteen, O. H., and Leven, N. L.: Arch. Surg. 22: 658, 1931.)

DISCUSSION

In Fig. 5 the gut is projected as a long straight tube. Obstruction of the gut in its upper reaches, where the digestive juices first enter it, is attended by essentially the same effects which accompany fistula at the same level. In either instance, and more effectually in obstruction than fistula, dehydration and dechlorination may be obviated by the liberal parenteral administration of water and sodium chloride. Whereas dogs with duodenal obstruction survive from two to four days ordinarily, if given generous amounts of saline solution subcutaneously, survival for as long as four weeks is not unusual.

Complete obstruction of the pelvic colon in dogs may be survived until the animal dies of starvation.[16, 17] Survival from forty to fifty

days has been reported. In man, as has previously been pointed out, however, complete obstruction of the colon not uncommonly terminates in perforation (and usually of the cecum) unless the obstruction is relieved by surgical decompression of the large bowel. Because of the competency of the ileocecal sphincter and because of the lengths of the lips of the valve, regurgitation into the lower reaches of the ileum frequently does not occur and a virtual closed loop obstruction ensues. It has been pointed out that such an obstruction may be unattended by vomiting and accompanied only by great distention and "gas pains." Despite the absence of fluid loss, such an obstruction is one of the most potentially hazardous of all simple obstructions.[14]

The results of the experiments here reported serve to shed light upon the somewhat enigmatic cause of death in obstructions involving the greater portion of the absorptive area of the gut. The majority of occlusions of the small intestine observed clinically concern its lower reaches in which the items of dehydration and dechlorination are not nearly so serious as in obstructions near the secretory level of the gut. Failure to prolong materially the survival of dogs with ileal obstruction by the parenteral administration of liberal quantities of saline solution has contributed considerably to general acceptance of the "toxic absorption factor" as the primary cause of death in ileal obstructions. Yet, the dog which possesses a relatively short small intestine may tolerate complete occlusion of the entire alimentary tract above it, if swallowed air is excluded. Exclusion of swallowed air permits such a segment even when obstructed to absorb the normal digestive juices. It is reasonable to assume that the same would hold true for man, particularly inasmuch as man has a relatively longer small intestine than the dog. At the same time, these experiments indicate the significance of increased intraluminal distention and tension (when swallowed air is not excluded). Evidence has been obtained which indicates that a sustained intraluminal pressure of 20 cm. of water, if maintained for twenty-two to twenty-eight hours, results in increased permeability owing to decreased viability of the gut wall. The avenue over which such abnormal absorption may occur in the presence of a damaged gut wall is probably the transperitoneal route,[12] though the experiments of Haerem, Dack, and Dragstedt with botulinus toxin would suggest increased absorption via normal avenues when the bowel is obstructed.[5]

SUMMARY

A method has been devised (cervical esophagostomy) by which ileal obstruction in dogs may be studied with exclusion of the swallowed air factor. In eleven such dogs (Table III) the average survival period

after the establishment of complete occlusion of the terminal ileum was thirty-six days. One dog survived for fifty-seven days. It was found that dogs in which a long closed loop of esophagus, stomach, and entire small intestine was made, absorbed the digestive juices when swallowed air was excluded. At autopsy the gut was usually found collapsed. The exclusion of swallowed air obviates the distention factor and in turn the sequelae of decreased viability and increased permeability which attend sustained increases of intraluminal pressure. These experiments indicate that complete occlusion of the terminal ileum may be well tolerated if the gut is not allowed to become distended by swallowed air. In effect, therefore, these experiments indicate that the mechanical factor of distention and not a "toxic factor" accounts for the lethal issue in ileal obstructions.

REFERENCES

1. Carlson, Herbert A., and Wangensteen, Owen H.: Histologic Study of the Intestine in Simple Obstruction, Proc. Soc. Exper. Biol. & Med. **29**: 421-424, 1932.
2. Gamble, J. L., and McIver, M. A.: A Study of the Effects of Pyloric Obstruction in Rabbits, J. Clin. Investigation **1**: 531, 1925.
3. Gamble, J. L., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, Ibid. **1**: 403, 1925.
4. Haden, R. L., and Orr, T. G.: Chemical Changes in the Blood of the Dog After Obstruction of the Duodenum, J. Exper. Med. **37**: 365, 1923; **38**: 55, 1923; **39**: 321, 1924.
5. Haerem, Sarah, Dack, G. M., and Dragstedt, Lester R.: Acute Intestinal Obstruction, SURGERY **3**: 339, 1938.
6. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs With Special Reference to Cause of Death and Treatment by Large Amounts of Normal Saline Solution, J. A. M. A. **59**: 82, 1912.
7. Hibbard, James S., and Wangensteen, Owen H.: Character of the Gaseous Distension in Mechanical Obstruction of the Small Intestine, Proc. Soc. Exper. Biol. & Med. **31**: 1063-1066, 1934.
8. McIver, M. A., Benedict, E. B., and Cline, J. W.: Postoperative Gaseous Distension of the Intestine, Arch. Surg. **13**: 588, 1926.
9. Morton, J. J.: The Differences Between High and Low Intestinal Obstruction in the Dog, Arch. Surg. **18**: 119, 1929.
10. Scott, H. G., and Ivy, A. C.: Jejunal Alimentation; an Experimental Study in Dogs, Ann. Surg. **93**: 1197, 1931.
11. Sperling, Louis: Effect of Previous Ileosigmoidostomy on Survival Period of Dogs with Low Ileal Obstruction, Proc. Soc. Exper. Biol. & Med. **31**: 323, 1933.
12. Sperling, Louis, and Wangensteen, Owen H.: Transperitoneal Absorption. VI. Significance of Impaired Viability and Influence of Distension on Its Occurrence, Proc. Soc. Exper. Biol. & Med. **32**: 1385-1389, 1935.
13. Wangensteen, Owen H.: The Early Diagnosis of Acute Intestinal Obstruction With Comments on Pathology and Treatment: With a Report of Successful Decompression of Three Cases of Mechanical Bowel Obstruction by Nasal Catheter Suction Siphonage, West. J. Surg. **40**: 1-17, 1932; Tr. West. S. A., 1931.
14. Wangensteen, Owen H.: The Management of Acute Intestinal Obstruction: With Special Mention of the Character of the Vomiting and Distension, Journal Lancet **54**: 640, 1934.

15. Wangensteen, Owen H.: The Therapeutic Problem in Bowel Obstructions, Springfield, Ill., 1937, Charles C. Thomas, Publisher.

16. Wangensteen, Owen H., and Chunn, Stanley S.: Studies in Intestinal Obstruction. III. Simple Obstruction: A Study of the Cause of Death in Mechanical Obstruction of the Upper Part of the Intestine, Arch. Surg. **16**: 1242, 1928.

17. Wangensteen, Owen H., and Leven, N. Logan: Correlation of Function With Cause of Death Following Experimental Intestinal Obstruction at Varying Levels, Arch. Surg. **23**: 658, 1931.

18. Wangensteen, Owen H., and Paine, John R.: Treatment of Acute Intestinal Obstruction by Suction With the Duodenal Tube, J. A. M. A. **101**: 1539, 1933.

CARCINOMA OF THE RIGHT COLON*

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FROM the standpoint of surgical diagnosis and treatment, carcinoma of the cecum, ascending colon, and hepatic flexure may be conveniently grouped under the general heading of carcinoma of the right colon. The clinical syndromes provoked by cancers in these several locations are essentially the same. They are frequently characterized by a severe secondary anemia even though there has been no visible loss of blood and also by the rarity of obstructive phenomena, both of which features stand in sharp contrast to the behavior of carcinomas of the left arm of the colon. Furthermore, carcinoma of the right colon is generally regarded as offering a better chance for cure than carcinoma at almost any other level of the digestive tract, this being due to the fact that these growths tend to remain localized for a long period of time. Metastasis to the regional lymph nodes and liver occurs at a relatively late stage in the life history of the disease, and, in this respect, the malignant growths of the right half of the colon differ considerably from cancers of the stomach, left colon, and rectum. Moreover, when surgical extirpation of a malignant lesion situated at any point in the right colon is to be performed, surgeons are quite generally agreed that right hemicolectomy is the procedure of choice. Cheever[1] mentions the following reasons for this: (1) Removal of a smaller segment of colon does not give a sufficiently wide margin of safety. (2) Due to the sacculated structure of the right colon and because it is devoid of peritoneum posteriorly, an anastomosis made here is less secure than one between the terminal ileum and the transversus, both of which are almost completely covered by peritoneum as well as being fairly mobile due to their respective mesenteries. (3) The ileum is provided with a good blood supply which minimizes the danger of suture-line necrosis with resultant leakage. (4) The operation is technically easier. Such a resection, of course, readily permits restoration of the intestinal continuity and a permanent artificial anus is not necessary. Concerning the exact details of the technique by which the operation can be best and most safely performed, there is no unanimity of opinion among different surgeons of considerable experience. Thus, some authors (Cheever,[1] Harvey[2]) favor a one-stage operation, consisting of resection of the right colon with a primary

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suture anastomosis between the terminal ileum and the proximal transverse colon. Others (Lahey and his associates[3]) prefer an obstructive type of resection for lesions in either the right or left colon, the procedure being essentially a modification of the original Mikulicz operation. Still others (Rankin,[4] Pemberton and Whittaker,[5] and Allen[6]) advise a two-stage operation, consisting first of an anastomosis between the low ileum and the transverse colon, to be followed by right hemicolectomy some three to six weeks later.

The present study is concerned with the cases of carcinoma of the right colon observed in the University Hospital from 1925 to 1937 and was undertaken, first, in order to make a careful analysis of the symptoms, signs, and complications in order thus possibly to clarify the early clinical picture of the disease; second, to evaluate the worth of the different operative procedures from the standpoint of mortality and postoperative complications; and third, to learn the end results of surgical treatment, both radical and palliative operations being considered. During this twelve-year period, the records of 91 cases of carcinoma situated in that segment of bowel between the ileocecal junction and the proximal transverse colon were found suitable for study. In the majority of these cases the diagnosis was verified by operation or necropsy and in these instances, histologic confirmation of the diagnosis was usually available. A certain few cases in which neither operation nor necropsy was performed were included, providing there was convincing clinical evidence in support of the diagnosis. Thus some cases having a compatible history with an abdominal tumor mass or positive x-ray and laboratory findings were accepted for study when thorough examination had also served satisfactorily to exclude other lesions.

ANATOMIC LOCATION

Table I gives the exact situation of the lesion in the right colon in the 91 cases. The cecum, as in the reports of other observers, was the section most commonly involved, while cancers of the hepatic flexure were second in frequency. It has been noted (McGlannan[7]) that the incidence of carcinoma at the hepatic and splenic flexures of the colon is slightly

TABLE I

CARCINOMA OF THE RIGHT COLON

ANATOMICAL LOCATION

LOCATION OF LESION	NUMBER OF CASES	PER CENT
Cecum	54	59.4
Ascendens	9	9.8
Cecum and Ascendens	10	10.9
Hepatic flexure	14	15.5
Ascendens and hepatic flexure	2	2.2
Entire right colon	2	2.2
	91	100.0

higher than in the adjacent portions of the bowel. The slight narrowing of the lumen and consequent stasis at these points have suggested the factor of chronic irritation by intestinal contents as a possible etiologic agent. For purposes of orientation, it is of interest to note that, during a two-year period, Hodges,[8] of the Department of Roentgenology of the University Hospital, on the basis of x-ray examination found carcinoma of the colon distributed as follows: pelvic colon (rectum and sigmoid), 60 per cent; left colon (distal half of transverse and the descending colon), 18 per cent; right colon (cecum, ascending colon, and proximal transverse colon), 22 per cent.

Thus, while carcinoma of the left colon (sigmoid and rectum being included) is the more important lesion by virtue of its more frequent occurrence, carcinoma of the right colon is deserving of careful study, since Allen in his review of the Massachusetts General Hospital cases found the operative mortality to be higher in this group of cases than in the resections performed on the left side.

In Table II are shown the age and sex incidence. With regard to sex, nothing remarkable is noted, it being common experience to find males affected more frequently than females, and in this series the ratio was approximately two to one. The study of the distribution of the cases according to age revealed that nearly 85 per cent occurred in the so-called cancer age from 40 to 70 years, and only 10 per cent were found in persons under 40 years of age. This is in rather striking contrast to our recent experiences with carcinoma of the left colon, rectum, stomach, and breast, when a surprisingly large number have been observed in patients between 20 and 40 years of age.

TABLE II

CARCINOMA OF THE RIGHT COLON

SEX AND AGE INCIDENCE

SEX	NUMBER OF CASES	PER CENT
	Sex Incidence	
Male	59	64.8
Female	32	35.2
Total	91	100.0

AGE	NUMBER OF CASES	PER CENT*
	Age Incidence	
11-20 inclusive	1	1.1
21-30 inclusive	1	1.1
31-40 inclusive	7	7.7
41-50 inclusive	19	20.9
51-60 inclusive	28	30.8
61-70 inclusive	29	31.8
71-80 inclusive	6	6.6
Total	91	100.0

*Mean, 55.22 years.

Since one of the purposes of the study was to summarize the significant symptoms and thus facilitate, if possible, earlier recognition of the disease, the chief symptoms of which these patients complained have been tabulated in Table III. It will be observed that some type of abdominal pain or distress was the most common chief complaint. The exact nature of the pain, its precise location, or the points to which it might radiate were neither constant nor characteristic and many variants of this complaint were noted.

TABLE III

CARCINOMA OF THE RIGHT COLON

CHIEF COMPLAINT

COMPLAINT	NUMBER OF CASES	PER CENT
Abdominal pain	37	40.6
Weakness	10	11.0
Abdominal pain and weakness	9	9.9
Diarrhea, abdominal pain and weakness	8	8.8
Constipation and abdominal discomfort	7	7.7
Tumor	6	6.6
Tumor and pain in right lower quadrant	6	6.6
Abdominal pain and vomiting	3	3.3
Abdominal distention and gas	3	3.3
No symptoms (accidentally discovered during routine examination)	2	2.2
Total	91	100.0
Appendectomy since onset of symptoms	10	11.0

Rankin states that the symptoms of carcinoma of the right colon may be divided into three main groups. The first is characterized by chronic digestive disturbances which tend to persist. Pain may be referred to the right upper quadrant of the abdomen, thus simulating chronic gallbladder disease, or to the right lower quadrant simulating chronic appendicitis. The second group is composed of symptoms referable to anemia. Thus, weakness, dyspnea, and pallor without other symptoms may be noted. Finally, there is a smaller group, in which an abdominal tumor mass first discovered by the patient or by the physician during a routine physical examination is the first indication of trouble. Comparing this classification with Table III, we find that these cardinal symptoms which Rankin describes appear here either singly or in combination. The 6 cases with unusual symptoms, such as vomiting and abdominal distention, were cases in which obstruction was present and the symptoms were those of the complicating intestinal obstruction rather than of the carcinoma itself. Of particular interest are the last 2 cases in the table, neither of these patients having had any symptoms referable to the abdomen but both found to have a carcinoma of the cecum during the course of a searching examination. One patient had come to the hospital because of an orthopedic condition and the other because of a cutaneous disorder. Since nearly three-fourths of the patients had abdominal pain as the chief complaint and since it not infrequently was

located in the right lower quadrant, it is perhaps not surprising that 10 patients, or 11 per cent of the group, had been subjected to appendectomy since the onset of symptoms and before hospital entry, a mistaken diagnosis of chronic appendicitis having been made.

A history of any change in the bowel habit of an individual is usually to be looked upon with suspicion, and, in teaching early diagnosis of cancer of the lower digestive tract, emphasis is placed upon the fact that any deviation from the normal for that individual, which tends to persist, calls for a thorough examination, including x-ray study by means of the barium enema. Such alterations in bowel habit may be in the nature of a tendency toward diarrhea or toward constipation. In our series, as far as could be told from a careful perusal of the case histories, no change in intestinal habit had been noted by the patient in half of the cases. Strangely enough, increasing constipation was considerably more common than diarrhea. The textbook symptom of alternating constipation and diarrhea was recorded in only six cases.

In the course of the routine history, patients were questioned specifically regarding any change in the appearance of the stools, and, as shown in Table IV, three-fourths of the patients denied having had bloody or tarry stools. This serves to emphasize the fact that a history of blood in the stool or on the stool is rarely obtained in cases of carcinoma of the right colon, and that a history of abnormal appearing stools is so uncommon that it will direct the attention of the examiner to the colon in only a small number of cases.

TABLE IV

CARCINOMA OF THE RIGHT COLON

SYMPTOMS

CHANGE IN BOWEL HABIT	NUMBER OF CASES	PER CENT
No change	44	48.3
Increasing constipation	24	26.4
Diarrhea	17	18.7
Alternating constipation and diarrhea	6	6.6
Total	91	100

ABNORMALITY OF STOOLS	NUMBER OF CASES	PER CENT
No change	68	74.7
Bloody	18	19.8
Tarry	5	5.5
Total	91	100

Table V presents the matter of weight loss in 82 cases in which the records were complete on that score. As might be expected, the great majority of patients had lost weight to some extent. As indicated in the table, in 65 per cent of the cases the amount of weight lost ranged between 10 and 40 pounds (4.6 to 18.2 mg.). Weight loss, then, as in the

case of cancer elsewhere and especially that of the gastrointestinal tract, is the rule, but unfortunately, because it is such a general symptom and one common to so many other chronic diseases, it does not assist greatly in arriving at an early diagnosis.

TABLE V

CARCINOMA OF THE RIGHT COLON

WEIGHT LOSS IN 82 CASES

NUMBER OF POUNDS	NUMBER OF CASES	PER CENT
No loss	5	6.1
1-10	7	8.5
11-20	19	23.4
21-30	20	24.4
31-40	14	17.0
41-50	6	7.3
51-60	2	2.4
61-70	2	2.4
71-80	0	0.0
81-90	0	0.0
91-100	1	1.2
Patient had lost weight but amount unknown	6	7.3
(No record	9)	

Table VI gives the time interval between the onset of symptoms and the date of admission to the hospital. These data are of interest since one fact which we were anxious to learn was during what stage of the disease most of the patients were applying for surgical treatment. We find from this survey that 25 per cent of the cases were seen within the first three months following the onset of symptoms; 45 per cent, within six months; and 70 per cent, within a year.

TABLE VI

CARCINOMA OF THE RIGHT COLON

DURATION OF SYMPTOMS BEFORE ADMISSION IN 86 CASES

TIME	NUMBER OF CASES	PER CENT
Less than 1 mo.	4	4.6
1- 3 mo.	18	20.9
4- 6 mo.	17	19.6
7-12 mo.	21	24.4
13-18 mo.	6	7.1
19-24 mo.	13	15.2
25-36 mo.	4	4.6
Over 3 yr.	3	3.6
Total	86	100

Clinical Findings.—In the clinical examination the presence of an abdominal tumor is probably the most important physical sign. As shown in Table VII, such a tumor mass was discovered in 72 per cent of the cases. If reference is made to Table III, it will be noted that 12 patients, or 13 per cent of the group, actually gave the presence of an abdominal tumor mass as a chief complaint.

TABLE VII

CARCINOMA OF THE RIGHT COLON

Physical Examination in 86 Cases

ABDOMINAL TUMOR	NUMBER OF CASES	PER CENT
Present	62	72.1
Absent	24	27.9
Stool Examination in 31 Cases		
OCCULT BLOOD	NUMBER OF CASES	PER CENT
Present	25	80.6
Absent	6	19.4
X-Ray Examination in 82 Cases		
	NUMBER OF CASES	PER CENT
Lesion demonstrated or suspected	72	87.8
Negative examination	10	12.2

Stool examinations were recorded in only 31 cases, but it is noteworthy that of this group the chemical tests for occult blood were positive in 80 per cent. This is of interest in view of the fact that, as was previously mentioned, 75 per cent of the patients gave no history of any gross abnormality of the stools.

Roentgen studies were made in 82 of the 91 cases and in 72, or 88 per cent, these were either positive for an intrinsic colonic lesion or the findings deviated from normal sufficiently at least to arouse the suspicion of the examiner and to raise the question of some abnormality in the bowel. Since this series of cases dates back to the time of the opening of the hospital in 1925, and in view of the great improvements in the technique of roentgen examination of the colon, it is probable that at the present time such a lesion can be demonstrated by a competent roentgenologist in at least 95 per cent of the cases.

Of the various laboratory examinations, the blood studies are of the chief interest. They are shown in Table VIII. It will be seen that a fairly marked anemia was present in most of the cases, as indicated by the mean hemoglobin reading of 57 per cent and the mean erythrocyte count of 3.76. In 1913[9] and again in 1921[10] W. J. Mayo pointed out that carcinoma of the right colon is more commonly associated with anemia than carcinoma of any other part of the body, with the exception of certain cancers of the stomach. Various explanations for this tendency to the production of anemia have been offered. Thus, it has been suggested that hemotoxins are formed; that the cecal mucous membrane is essential to a normal blood picture; that the anemia is related to the high degree of malignancy of these tumors; that it is associated with chronic intestinal obstruction, weight loss, or hemorrhage. This matter has been extensively studied by Alvarez and his associates. They find that there is a definite relationship between the area of the tumor removed at operation and the degree of the anemia and emphasize the fact that nowhere else in the interior of the body are ulcerating cancers found as large as those in the cecum. Furthermore, nowhere else are

TABLE VIII

CARCINOMA OF THE RIGHT COLON

BLOOD STUDIES

HEMOGLOBIN DETERMINATION	NUMBER OF CASES	ERYTHROCYTE COUNT	NUMBER OF CASES
15- 19	2	1.5-1.9	2
20- 24	4	2.0-2.4	3
25- 29	3	2.5-2.9	6
30- 34	2	3.0-3.4	9
35- 39	1	3.5-3.9	8
40- 44	8	4.0-4.4	14
45- 49	4	4.5-4.9	11
50- 54	9	5.0-5.4	3
55- 59	11	5.5-5.9	0
60- 64	9	6.0-6.4	1
65- 69	6	No record	34
70- 74	5	Mean 3.76	
75- 79	6		
80- 84	5		
85- 89	4		
90- 94	1		
95-100	2		
No record	9		
Mean 57.6			

such large raw surfaces constantly bathed in a fluid medium containing a concentrated culture of the most virulent organisms. Hence they conclude that there is nothing about the cecum or its mucous membrane which is essential to the hematopoietic system and that the explanation of the anemia lies in the presence of a large ulcerated surface from which blood can ooze and through which bacteria can enter. Rankin and Graham,[12] on the other hand, believe that the anemia is probably due to some perverted or inhibited function of the mucous membrane which allows toxins to be readily absorbed. In support of this contention they quote the work of Whipple, Schmidt, Koons, and others.

In order to determine whether the degree of anemia was an index of the extent of the lesion and therefore a criterion of operability, all cases explored surgically as well as those judged hopelessly inoperable when first seen were combined and divided into three groups, depending upon the hemoglobin readings. In 15 cases the hemoglobin was between 15 and 44 per cent; in 37 it was between 45 and 69 per cent; and in 22 it was over 70 per cent. The number of cases in which resection was possible in these three groups was 6, 20, and 10 respectively. Thus, as had been expected, the lowest resectability (40 per cent) was found in the group with the most severe anemia. However, in the middle group, with a hemoglobin range from 45 to 69 per cent, the operability was found to be the highest (54 per cent) while in the cases in which there was only a slight degree of anemia (hemoglobin 70 per cent or higher) the resectability was second highest (45 per cent). The best explanation for this seems to be that in this last group of cases there were some of

the less differentiated or more malignant tumors, which tended to metastasize early or to infiltrate extensively, while in this group also were found some of the smaller tumors which showed complications, such as perforation or obstruction at an early date. Hence, in general, it would seem that a severe degree of anemia denotes an advanced and often an inoperable lesion, but the degree of the anemia and the resectability do not run entirely parallel with one another.

TABLE IX

CARCINOMA OF THE RIGHT COLON

RESECTABILITY IN RELATION TO DEGREE OF ANEMIA IN 74 CASES

HEMOGLOBIN READING	NUMBER OF CASES	NUMBER OF CASES RESECTABLE	PER CENT
15- 44	15	6	40.0
45- 69	37	20	54.0
70-100	22	10	45.4

Treatment.—Table X shows in outline form the disposal which was made of the 91 cases. In 15 the lesion was thought to be operable but operation was refused. These patients either refused treatment entirely or went elsewhere. Eight cases were frankly inoperable and no treatment of any kind seemed worthwhile. Thirty-two cases, at the time of laparotomy, were found to have extensive infiltration into adjacent structures, hepatic or other distant metastases, or various conditions contraindicating any radical procedure. In 5 of the 32 the operation consisted of simple exploration with biopsy when possible. In 20 an ileocolostomy between the low ileum and the transverse colon was performed. In 2 ileosigmoidostomy was necessary because of involvement of the transverse colon. The 5 instances of enterostomy or cecostomy were advanced cases of acute intestinal obstruction and emergency operation was performed for the relief of the obstruction.

TABLE X

CARCINOMA OF THE RIGHT COLON

OPERABILITY

TREATMENT	NUMBER OF CASES	PER CENT
Operation advised; patient refused	15	16.4
Inoperable	8	8.8
Palliative operation	32	35.2
Ileotransverse colostomy	20	22.0
Ileosigmoidostomy	2	2.2
Cecostomy and enterostomy	5	5.5
Exploration only	5	5.5
Radical operation (resection)	36	39.6
Resection with primary suture anastomosis	25	27.5
Obstructive resection	6	6.6
Two-stage operation	5	5.5
Total	91	100.0
Resectability in 76 cases = 47.6%		

Resection was possible in 36 cases and if the 15 patients who refused treatment are disregarded, the resectability was 47.6 per cent. Undoubtedly in the group of 15 who refused treatment there were some favorable cases. Thus it seems reasonable to suppose that the resectability for the entire group was approximately 50 per cent.

The 20 palliative ileotransverse colostomies were all side-to-side lateral anastomoses. In some of these cases a proximal catheter enterostomy was added as a form of safety valve for the purpose of relieving tension on the suture line. More recently this practice has been abandoned, as it is now regarded an unnecessary precaution. As shown in Table XI, the mortality was considerably higher when the enterostomy was performed. The reason for this was usually some form of infection, either general peritonitis, or severe wound sepsis which often resulted in a persistent fecal fistula. Thus, we believe that the complementary proximal enterostomy in such cases is not only unnecessary but unwise.

TABLE XI

CARCINOMA OF THE RIGHT COLON

PALLIATIVE OPERATIONS

TYPE OF OPERATION	NUMBER OF CASES	LIVED	DIED	MORTALITY PER CENT
Ileotransverse colostomy	20	14	6	30.0
Lateral anastomosis without proximal enterostomy	13	11	2	15.4
Lateral anastomosis with proximal enterostomy	7	3	4	57.0
Ileosigmoidostomy	2	1	1	50.0
Cecostomy and enterostomy	5	1	4	80.0
Exploration only	5	4	1	20.0

The high mortality of 80 per cent in the small group of cases in which enterostomy or cecostomy was performed is not surprising. These were all far-advanced cases, and an attempt was made to relieve the acute obstruction even though the risk was great.

The radical operations fall into three main groups: (1) resection of the right colon with some form of primary suture anastomosis; (2) obstructive resection; and (3) a two-stage operation, consisting of ileotransverse colostomy as the first stage, followed by right hemicolectomy, after the function of the anastomosis was well established, usually about three weeks later.

In the first group of one-stage operations, with primary suture anastomoses, the anastomosis was of the side-to-side variety in 12, end-to-end in 9, and end-to-side in 4. In the two latter types a proximal enterostomy was always performed. This was also done in 6 of the 12 lateral anastomoses, while in the remaining 6 it was not thought necessary. Here again, the experience was the same as in the group of palliative side-tracking operations, i.e., the results were much superior when an enterostomy was not done. We, therefore, believe that if a one-

stage resection is to be performed the strongest possible type of anastomosis should be employed in order to avoid the necessity of a complementary enterostomy. Such an anastomosis is undoubtedly the side-to-side type.

In this group of cases adequate statistical data are not available with reference to the relative merits of the different so-called aseptic types of anastomosis. In nearly one-half of the cases the anastomosis was made according to the Parker-Kerr basting-stitch technique or with the aid of the Furniss clamp. In the remainder of the cases an open anastomosis was performed. It is our belief, however, that the aseptic type of anastomosis has much to recommend it, and we continue to employ it when technically feasible.

While most surgeons are agreed that obstructive resection is a suitable procedure for lesions in the left colon, relatively few advocate its use on the right side. The chief objection to its use here is the fact that, during the interval between the actual resection and the time when the temporary intestinal fistula can be closed, the patient is handicapped by a complete ileostomy. While it may not be a serious argument against the use of this method, nevertheless the excoriation of the skin and the uncontrollable watery discharges are far more distressing and incapacitating than in the case of a temporary sigmoid or transverse colostomy. In the present series the number of patients treated by this method is so small that statistical data are of little value. However, in the figures available for comparison, the mortality proved to be essentially the same as for the one-stage resections, that is, approximately 32 per cent.

Likewise, the two-stage operation was utilized in only a small number of cases, and hence our experience with this procedure is limited. It is a method which has long been advocated by Rankin for patients who are not first-class surgical risks, and its various advantages have recently been emphasized by Pemberton and Allen. The chief reasons for employing a two-stage procedure are: first, that the amount of operating done at any one time is considerably decreased; and second, that the preliminary ileocolostomy confers upon the peritoneum a certain degree of immunity to infection so that the hemicolectomy can be done more safely. As Pemberton has pointed out, the first stage of the procedure is quite effective in sealing off the left side of the abdomen by adhesions. Thus, the second stage can be done with scarcely any exposure or handling of the small intestine. The added safety made possible by this method seems to more than compensate for any disadvantages that it may have. Most important of these disadvantages is probably the longer period of hospitalization. In spite of a two-stage procedure, however, the total number of hospital days is not greatly increased because the convalescence following each stage is usually smooth and uneventful; whereas, in the one-stage operation it is apt to be prolonged

and often stormy. The added hazard of the administration of two anesthetics and the danger of postoperative complications in two postoperative periods have probably been greatly overemphasized in the past. It is true, of course, that the malignant growth is left in situ, during the interval of two or three weeks between stages, and, theoretically at least, it is capable of giving rise to metastases during this time. However, in view of the slow rate of growth of these colonic cancers, with metastasis taking place at a late stage of the disease, no great harm seems likely on this score. Furthermore, as the result of putting the tumor-containing bowel segment at rest by means of the ileocolostomy, there is a marked subsidence of infection, and the tumor mass may decrease in size so that its subsequent removal becomes safer and easier.

The optimal interval of time between the two stages is generally believed to be about three weeks; i.e., a sufficiently long period to allow the anastomosis to become firmly healed and its function well established. As to the time when the maximum degree of immunity of the peritoneum is attained, there is considerable difference of opinion. At the present time we are attempting to show when this occurs in experimental animals and these results will be the basis of a separate publication.

As indicated in Table XII, the lowest operative mortality followed the use of the two-stage operation. In this small group of cases there were two patients over 70 years of age, one 71 and the other 78, and both of them made a satisfactory convalescence. Furthermore, since this study was completed, 5 additional cases have been treated by this method with successful outcome, thus improving considerably the results shown in the table. We now believe that the two-stage operation should not be reserved for the poor surgical risk, but that it is the preferable procedure for most patients with malignant disease. Undoubtedly there are some patients who are able to withstand a one-stage operation

TABLE XII

CARCINOMA OF THE RIGHT COLON

RADICAL OPERATIONS

TYPE OF OPERATION	NUMBER OF CASES	LIVED	DIED	MORTALITY PER CENT
Resection with primary suture anastomosis	25	17	8	32.0
Lateral anastomoses	12	9	3	25.0
Lateral anastomoses without enterostomy	6	6	0	0.0
Lateral anastomoses with enterostomy	6	3	3	50.0
End-to-end anastomosis (with enterostomy)	9	7	2	22.2
End-to-side anastomosis (with enterostomy)	4	1	3	75.0
Obstructive resection	6	4	2	33.3
Two-stage operation	5	4	1	20.0
Total	36	25	11	30.06

and this is particularly true when the resection is done for some lesion other than carcinoma. However, these are the exceptional cases and require very careful selection.

Table XIII gives the cause of death in all of the radical operations ending fatally. While general peritonitis was present in about one-half of the cases, it alone was not responsible for the fatal outcome as frequently as one might suppose. With greater standardization of the operative procedures and a fairly long meticulous preoperative preparatory regime, the incidence of general peritonitis has been very greatly reduced. Fatal cardiovascular or renal disorders were not uncommon. A considerable number of the deaths were due to those postoperative complications, especially pulmonary, which are common to all major

TABLE XIII

CARCINOMA OF THE RIGHT COLON

CAUSE OF DEATH FOLLOWING RADICAL OPERATIONS

	AUTOPSY
Resection with primary suture anastomosis	
Case 1. Pneumonia, wound sepsis	+
Case 2. Pneumonia, wound sepsis	+
Case 3. General peritonitis	+
Case 4. Paralytic ileus, cardiac failure, pneumonia	+
Case 5. General peritonitis	−
Case 6. Peritonitis, pneumonia	−
Case 7. Erysipelas, uremia	−
Case 8. Transfusion reaction	−
Obstructive resection	
Case 1. Gangrene ileal stump, general peritonitis, pneumonia	+
Case 2. Coronary occlusion	+
Two-stage operation	
Case 1. General peritonitis, pneumonia	+

surgical procedures carried out in patients of this age group. While the use of spinal rather than inhalation anesthesia may assist in reducing the incidence of postoperative pneumonia, probably more important is the constant attention to minute details in the postoperative care. Thus, encouraging the patient to cough, frequent changes of posture, hyperventilation by means of carbon dioxide inhalations, and the avoidance of too tight abdominal dressings are all points worthy of attention. Wound sepsis is an important postoperative complication and when it occurs in these debilitated patients, it not infrequently results fatally. On the basis of the experimental studies on vitamin C deficiency and wound healing made by Lanman and Ingalls,[13] Allen recommends the use of cevitamic acid and of liver extract intramuscularly both before and after operation, in order to favor normal wound healing.

We have been impressed with the rather marked decrease in the incidence of infected laparotomy wounds following the use of nonabsorbable suture material. Thus, in this type of case the results of closure of the

peritoneum with interrupted silk sutures and of the fascia with either silk or the Babcock alloy steel wire, in our hands, have been very gratifying.

In Table XIV are listed the important complications of the disease which were present at the time of hospital entry. The incidence of obstruction, either acute or subacute, was somewhat higher than had been expected. When obstruction was present, it was usually due either to a large cecal growth so situated as to occlude the ileocecal junction, thus producing small intestinal obstruction, or else it was an advanced carcinoma situated at or near the hepatic flexure.

TABLE XIV

CARCINOMA OF THE RIGHT COLON

PATHOLOGY

COMPLICATIONS	NUMBER OF CASES	PER CENT
Perforation with abscess	2	2.2
Perforation with general infection	2	2.2
Acute or subacute intestinal obstruction	10	11.0
Duodenocolic fistula	1	1.1
Incidence of Metastasis to Regional Lymph Glands in 25 Specimens		
Glands involved	11	44.0
Glands not involved	14	56.0

The matter of regional lymph node involvement is of interest, since it is commonly believed that carcinoma of the cecum, for example, metastasizes at a later date than carcinoma elsewhere in the digestive tract. Important observations have been made by Craig and MacCarty,[14] Hayes,[15] and McVay.[16] In 300 sections of colon resected for carcinoma, these authors isolated and studied microscopically the included lymph nodes. They found an increasing tendency for the lymph nodes to be involved in passing from the cecum to the rectum. Thus, the regional glands were positive in 47 per cent of the rectal cancers; whereas, involvement was present in only 32 per cent of the cecal growths. In the case of lesions situated between these two points, there was a fairly even gradation in metastasis. While complete records of nodal involvement were not available in all of the cases in the present study, microscopic examination of the regional lymph nodes was made in 25 of the resected specimens. The glands were uninvolved in 14, or 56 per cent, and positive in the remaining 11, or 44 per cent.

Table XV shows the end results of palliative ileocolostomy in the 15 patients upon whom this operation was performed and who were discharged from the hospital alive. It was possible to trace all of the cases and all had died.

The exact duration of life following operation is given in Table XVI. Whether such palliative operations are worth while depends considerably upon the circumstances and the problems presented by the individual case. It is certainly true that an average postoperative life expectancy

TABLE XV

CARCINOMA OF THE RIGHT COLON

END RESULTS OF PALLIATIVE OPERATION IN 15 CASES (ALL TRACED)

LIVED	NUMBER OF CASES	PER CENT
Less than 3 mo.	3	20.0
3- 7 mo.	6	40.0
7-10 mo.	5	33.3
Over 10 mo.	1	6.7
	15	100.0
Average length of life following operation	6.6 mo.	
Longest survival period	20 mo.	
Shortest survival period	1½ mo.	

of 6.6 months is not very much to hold out in the way of hope, yet the temporary symptomatic improvement often noted, the protection against acute obstruction, and the frequent improvement in the anemia as well as occasional survival periods of 1½ to 2 years, would seem to justify the procedure. It is of interest to place upon record these results as in this clinic we have been engaged for some time in conducting a survey of the end results of the various palliative operations for the different types of abdominal carcinoma. We have now accumulated such data for carcinoma of the stomach,[17] pancreas,[18, 19] and rectum.[20]

TABLE XVI

CARCINOMA OF THE RIGHT COLON

END RESULTS OF RADICAL OPERATIONS IN 25 CASES (ALL TRACED)

LIVED	NUMBER OF CASES	PER CENT
6 mo. or less	1	4.0
7-12 mo.	1	4.0
13-18 mo.	1	4.0
19-24 mo.	4	16.0
25-30 mo.	1	4.0
31-36 mo.	1	4.0
Over 3 yr.	3	12.0
Still living	13	52.0
	25	100.0
Longest survival period of patients now dead	4 yr.	
Shortest survival period of patients now dead	4½ mo.	
Average survival period of patients now dead	26¼ mo.	

It was likewise possible to follow all of the patients upon whom radical operations were performed. Half of the patients were found to be still living, and in the case of those who had died the average duration of life was 26½ months. The deaths were all checked with the vital statistics of the State Department of Health. While it is quite possible that death was due to causes other than recurrence, in a certain few of the cases, as a rule the circumstances of death as recorded on the death certificates leave little doubt that death was due either to a recurrence of the disease or to distant metastases. While these results of treatment

TABLE XVII

CARCINOMA OF THE RIGHT COLON

PATIENTS STILL LIVING FOLLOWING RADICAL OPERATION

Case 174403 is alive at the end of	3 mo.
Case 391863 is alive at the end of	6½ mo.
Case 389384 is alive at the end of	10 mo.
Case 390943 is alive at the end of	10½ mo.
Case 192307 is alive at the end of	11 mo.
Case 348964 is alive at the end of	2 yr., 9 mo.
Case 297753 is alive at the end of	3 yr., 3 mo.
Case 335881 is alive at the end of	3 yr., 4 mo.
Case 248994 is alive at the end of	4 yr., 1½ mo.
Case 303540 is alive at the end of	4 yr., 9 mo.
Case 262022 is alive at the end of	6 yr., 4 mo.
Case 226372 is alive at the end of	8 yr.
Case 187393 is alive at the end of	10 yr.

are not brilliant, nevertheless, the fact that one patient was found to be living and well at the end of ten years and another at the end of eight years shows that cure is possible by radical surgery. Of the 13 patients still living, 3 have survived for more than five years. Thus there were five-year cures in 12 per cent of all of the radical operations performed, or 3.3 per cent of the entire group of 91 cases.

SUMMARY AND CONCLUSIONS

1. The case records of 91 cases of carcinoma of the right colon observed in the University Hospital, during the twelve-year period from 1925-1937, have been reviewed and analyzed.

2. Carcinoma of the right colon was considerably less common than of the left colon. Over one-half of the cancers of the large bowel were found to be situated in the sigmoid and rectum. In the right colon carcinoma was considerably more common in the cecum than in the ascendens or hepatic flexure.

3. Males were affected more frequently than females, the ratio being approximately two to one. Over 80 per cent of the cases occurred in individuals between 40 and 70 years of age. The mean age was 55.22 years.

4. Some form of abdominal pain or discomfort was the most common chief complaint. Because of pain located in the right side of the abdomen or in the right lower quadrant, 10 patients, or 11 per cent of the group, had had appendectomies performed prior to admission to the hospital.

5. Approximately one-half of the patients gave no history of change in bowel habit. One-fourth complained of increasing constipation. Only 6.6 per cent gave a history of alternating constipation and diarrhea. Likewise three-fourths of the patients gave no history of abnormal appearing stools.

6. Nearly all patients gave a history of weight loss. In 65 per cent of the cases the amount ranged from 10 to 40 pounds (4.6 to 18.2 kg.).

7. Approximately 25 per cent of the patients came to the hospital within three months following the onset of symptoms; 45 per cent, within six months; and 70 per cent, within one year.

8. An abdominal tumor mass was noted on physical examination in nearly three-fourths of the cases.

9. In the group of 31 cases in which the guaiac and benzidine tests were performed, occult blood was found in the stools in 80 per cent.

10. Of 82 cases examined roentgenologically, the lesion was demonstrated or its presence was suspected in 88 per cent.

11. The mean hemoglobin reading for the group was 57 per cent. The mean erythrocyte count was 3.76.

12. The degree of the anemia was not necessarily a criterion of resectability. The lowest resectability occurred in the cases with the most marked anemia (15 to 44 per cent Hg). The highest resectability was found in the intermediate group (45 to 69 per cent Hg).

13. Palliative operations were performed in 32 cases, or 35.2 per cent of the group. Radical operations were possible in 36 cases, or 39.6 per cent. The resectability in 76 cases (excluding 15 patients who refused operation) was 47.6 per cent.

14. The most useful palliative operation was ileotransverse colostomy for the purpose of excluding the involved bowel segment and preventing obstruction in the future. The operative mortality in 20 cases was 30.0 per cent. The mortality was considerably higher when a proximal catheter enterostomy was performed simultaneously than when it was omitted.

15. Among the radical operations, while the number of cases in any one group is too small to make statistical comparisons of great value, the two-stage operation seems to be superior to any form of one-stage procedure, judging from operative mortality (20 per cent). Obstructive resections and one-stage resections with primary suture anastomoses, in general, carried about the same mortality; viz., 33 per cent.

16. Perforation of the bowel was a relatively uncommon complication, occurring in only 4.4 per cent of the cases. Acute or subacute intestinal obstruction, on the contrary, was somewhat more frequent than had been anticipated. It was noted in 10 cases, or 11 per cent of the group.

17. In 25 resected specimens in which microscopic study of the regional lymph nodes was made, metastases were found in the regional lymph nodes in 44 per cent, while the glands were uninvolved in 56 per cent.

18. A follow-up study of the 15 palliative short-circuiting operations showed the average duration of life following operation to be 6.6 months. The longest period of survival was 20 months and the shortest 1½ months.

19. A follow-up study of the 25 radical operations showed that 12 patients were dead, in all probability due to recurrence of the disease. The average survival period for this group was 26½ months. Of the patients still living and well, there were 3 five-year cures; i.e., 12 per cent of the radical operations performed, or 3.3 per cent of the entire group of 91 cases.

REFERENCES

1. Cheever, David: The Choice of Operation in Carcinoma of the Colon, Ann. Surg. **94:** 705, 1931.
2. Harvey, Samuel C.: The One-Stage Operation for Resection of the Cecum and Proximal Colon, New England J. Med. **211:** 1038, 1934.
3. Lahey, Frank H.: Resection of Right Colon and Anastomosis of Ileum to Transverse Colon After Mikulicz Plan, Surg., Gynec. & Obst. **54:** 923-929, 1932; New England J. Med. **206:** 315-322, 1932.
4. Rankin, Fred W.: Surgical Lesions of the Large Bowel, J. Michigan State M. Soc. **31:** 1, 1932.
5. Pemberton, J. de J., and Whittaker, L. D.: Resection of the Right Half of the Colon, Surg., Gynec., and Obst. **65:** 92, 1937.
6. Allen, Arthur W.: Right Colectomy for Malignant Disease—A Discussion of the Mortality Associated With Various Operative Procedures, J. A. M. A. **109:** 923-927, 1937.
7. McGlannan, Alexius: Diseases of the Colon (Carcinoma), Dean Lewis' Practice of Surgery, Hagerstown, Md., 1929, Chapter IV, Vol. VII, pp. 68, 69.
8. Hodges, Fred Jenner: Disease of the Colon, Wisconsin M. J. **34:** 821-825, 1935.
9. Mayo, W. J.: Some of the Disputed Problems Associated With Surgery of the Large Intestine, Am. J. M. Sc. **145:** 157, 1913.
10. Idem: Pernicious Anemia With Special Reference to the Spleen and the Large Intestine, Ann. Surg. **74:** 355, 1921.
11. Alvarez, Walter C., Judd, E. Starr, MacCarty, William C., and Zimmermann, Arnold R.: The Varying Degrees of Anemia Produced by Carcinoma in Different Parts of the Colon, Arch. Surg. **15:** 402, 1927.
12. Rankin, Fred W., and Graham, A. Stephens: Carcinoma of the Colon, Christopher, Textbook of Surgery, Philadelphia, 1936, W. B. Saunders Co., p. 1245.
13. Lanman, Thomas, and Ingalls, Theodore H.: Vitamin C. Deficiency and Wound Healing, an Experimental and Clinical Study, Ann. Surg. **105:** 616, 1937.
14. Craig, W. M., and MacCarty, W. C.: Involvement of the Lymph Glands in Cancer of the Cecum, Ann. Surg. **77:** 698, 1923.
15. Hayes, J. M.: The Involvement of the Lymph Glands in Carcinoma of the Large Intestine, Minnesota Med. **4:** 653, 1921.
16. McVay, J. R.: Involvement of Lymph Nodes in Carcinoma of the Rectum, Ann. Surg. **76:** 755, 1922.
17. Ransom, Henry K., and Coller, Frederick A.: Carcinoma of the Stomach: Observations on Surgical Treatment, J. Michigan State M. Soc. **31:** 87-92, 1932.
18. Coller, Frederick A., and Winfield, James M.: Evaluation of Palliative Operation for Cancer of the Pancreas, Am. J. Surg. **25:** 64-69, 1934.
19. Ransom, Henry K.: Carcinoma of the Body and Tail of the Pancreas, Arch. Surg. **30:** 584-606, 1935.
20. Coller, Frederick A., and Ransom, Henry K.: The One-Stage Procedure of the Treatment of Carcinoma of the Rectum, Ann. Surg. **104:** 636-645, 1936.

ACUTE PANCREATITIS

A Report of 26 Cases

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ACUTE pancreatitis has been described as being one of the most dramatic of all diseases. It has been placed in the same category as ruptured ectopic pregnancy, since, in both, the classical description is one of profound shock. This impression in the latter instance has been changing because now most patients with ectopic pregnancy are operated upon before the lesion ruptures. In pancreatitis, however, many physicians are still reluctant to make the diagnosis in the absence of shock and cyanosis. An analysis of the cases here presented demonstrates that such findings are quite unusual. It was the relative mildness of symptoms and findings in severe cases in contrast to the classical description that aroused interest and prompted a study of our case records. We have noted that increased interest in the subject has brought about improved results in both the diagnosis and treatment of our own cases; for example, the three cases seen after this work was started were correctly diagnosed preoperatively.

The study covers twenty-six patients with acute pancreatitis operated upon at the Henry Ford Hospital. Cases not coming to operation and those definitely secondary to a perforating peptic ulcer are not included.

Pathogenesis.—The experimental work on acute pancreatitis is enormous in volume. The most comprehensive contributions in recent years are those of Wangensteen, in 1931, and of Dragstedt, in 1934. The work of the former was confined largely to pathogenesis, while the latter considered the cause of death as well. These phases of the subject have been the chief points of interest for many years.

Without rehashing the great bulk of material which is readily available, it may logically be stated that no one factor can be considered the etiological agent in all cases. Bile must still be accepted as the most important factor. Dragstedt concluded that 60 per cent could be explained on the old common channel theory, 10 per cent of these being caused by stone in the ampulla and the remainder by spasm or edema of the sphincter of Oddi as suggested by Archibald. Because of the impossibility of demonstrating a common channel in certain proved cases of pancreatitis, the bile factor has been severely censored and many fantastic theories promulgated. However, it must be accepted as the

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most frequent causative agent of pancreatitis. In the remaining 40 per cent of cases lymphogenous, hematagenous, or ductal spread of infection must be considered. Vascular injury will also produce pancreatitis, as will physical trauma. The protected position of the organ lessens the danger from trauma, but many interesting cases of rupture and repair are reported.

Incidence.—Acute pancreatitis is a rare disease. From 1916 to 1937, inclusive, there were 268,293 patients admitted to the Henry Ford Hospital and of this number only 26 were operated upon for acute pancreatitis. Thus, there was only 1 patient with acute pancreatitis for each 10,000 admissions.

Seasonal Incidence.—Acute pancreatitis does not appear to have the definite seasonal variation that is demonstrable in so many diseases. The incidence by seasons of our cases is shown in Table I.

TABLE I

ACUTE PANCREATITIS

SEASONAL INCIDENCE

SEASON	NO. OF PATIENTS	PERCENTAGE
Spring	8	30.8
Summer	7	26.9
Fall	4	15.4
Winter	7	26.9
	26	100.0

Sex.—There were 14 males and 12 females in the group studied. This observation may be used as an argument against the relationship of gallbladder disease, since cholecystitis is much more common in females than in males in the proportion of 3 to 1. In 301 cases of acute cholecystitis operated upon here during the same period, there were 89 males and 212 females.

Race.—The colored race had only 1 representative.

Nationality.—There were 20 Americans, 2 Poles, 1 Italian, 1 Austrian, 1 Englishman, and 1 Canadian.

TABLE II

ACUTE PANCREATITIS

AGE

DECADE	AGE	NO. OF PATIENTS	PERCENTAGE
1	0- 9	0	0.0
2	10-19	1	3.8
3	20-29	5	19.3
4	30-39	3	11.5
5	40-49	9	34.6
6	50-59	5	19.3
7	60-69	2	7.7
8	70-79	1	3.8
		26	100.0

Age.—Acute pancreatitis may occur at any age. Its association with acute infection in childhood, especially mumps, has been stressed by Farman. Table II shows that 2 patients in this small series were under 20 years of age and that 3 of them were over 60 years old. More than one-third of the patients were between the ages of 40 and 49 and over one-half of them between the ages of 40 and 60. This finding is in support of the theory of relationship to gall-bladder disease, since this period is the gall-bladder age.

Weight.—It has been stated that patients with acute pancreatitis are usually obese. Table III indicates that, while slightly more than one-third of the patients whose avoirdupois was recorded preoperatively weighed more than 175 pounds, exactly one-half of them weighed less than 150 pounds.

TABLE III

ACUTE PANCREATITIS

WEIGHT

WEIGHT IN LB.	NO. OF PATIENTS	PERCENTAGE
100-125	1	6.3
126-150	7	43.7
151-175	2	12.5
175-200 plus	6	37.5
Total as recorded	16	100.0
Unrecorded	10	
Total patients	26	

HISTORY

Previous Gastrointestinal History.—Only 10 of the patients, or 38.5 per cent of the series, gave a history that was negative for gastrointestinal symptoms. All of the remaining 16 patients had complained of symptoms which had led their medical adviser to suspect gall-bladder disease, but a positive diagnosis by biliary drainage or cholecystogram study had been made on only 3 patients. A history of an attack similar to the present one was obtained from 14 patients, or 53.8 per cent of the series. Seven of the patients had been jaundiced previously; 5 had suffered from bloating; 2, from upper abdominal distress after meals; 2, from fat intolerance; 2, from hives; and 2, from constant pain in the gall-bladder region. One patient complained of persistent vague digestive disturbance; 1, of hunger pain; and 1 of the group had had an appendectomy for a gangrenous appendix four months previously.

Subjective Symptoms.—The history commonly elicited was very similar to that of any other acute intra-abdominal catastrophe. Twenty-three of the patients had severe pain as the outstanding symptom, while in only 3 instances, or 11.5 per cent, was the pain classified as moderate. In 23 patients the pain was in the epigastrium; 2, at the umbilicus; and in 1 the only pain complained of was in the right lower quadrant. In

all three of these unusual locations the pain was severe. Free blood in the peritoneal cavity, pooled in the right lower quadrant, may account for the location in the last instance, but does not give any reason for the absence of upper abdominal pain. No explanation is apparent in the two instances with localization at the umbilicus.

While pain was noted in all cases, nausea was absent in only 1 and actual vomiting occurred in 24. In 1 the vomitus was continually streaked with blood and in another in which obstipation and distention were marked, the vomitus was considered to be fecal in nature. No special comment could be made in regard to the vomiting in the remainder, except that it was repeated. Beyond pain, nausea, and vomiting, no other persistent symptoms were noted. An analysis of the isolated occurrence of interesting symptoms, as noted in Table IV, indicates the relative lack of pathognomonic symptoms. The story as given by the patient is not of any great help in arriving at a diagnosis in practically 100 per cent of the cases considered. The onset of steady pain, reaching its acme early, is the possible exception.

TABLE IV

ACUTE PANCREATITIS

RARER SYMPTOMS

SYMPTOM	NO. OF PATIENTS	PERCENTAGE
Pain in right shoulder	2	7.7
Pain in left shoulder	1	3.8
Pain in back	1	3.8
Chills and fever	2	7.7
No bowel movement for 2 days	1	3.8
Diarrhea	2	7.7
Abdominal distention of notable degree	4	15.4
Cold and clammy sensation	1	3.8
Cold sweats	1	3.8
Pregnancy (6 months' duration)	1	3.8
Puerperal state (3 days)	1	3.8

CLINICAL FEATURES

A survey of the findings on physical examination is somewhat more encouraging, since the objective symptoms demonstrate a tendency to uniformity and so provide clues of diagnostic value.

Temperature.—Table V indicates the temperature reading before operation. A subnormal temperature was recorded in 19.3 per cent of the patients and in 53.9 per cent the reading was not above 100° F. Elevation above 102° F. was noted in only 7.7 per cent. The inference is that infection plays a minor role in the etiology of acute pancreatitis.

Pulse Rate.—The pulse rate of the patient with acute pancreatitis, as recorded in Table VI, may be taken as an index of the degree of involvement of the pancreas. The pulse rate is surprisingly low. In a total of 38.5 per cent of the patients the rate was under 100 and in only

TABLE V

ACUTE PANCREATITIS

TEMPERATURE

F. READING	NO. OF PATIENTS	PERCENTAGE
96.0-98.6	5	19.3
98.8-100	9	34.6
100.2-101	7	26.9
101.2-102	3	11.5
102.2-103	0	0.0
103.2-104	2	7.7
	26	100.0

23.1 per cent was it over 120. This finding is at variance with the older concepts of the disease, in which shock was stated to be an outstanding symptom.

TABLE VI

ACUTE PANCREATITIS

PULSE RATE

RATE	NO. OF PATIENTS	PERCENTAGE
60- 70	2	7.7
70- 80	1	3.8
80- 90	2	7.7
90-100	5	19.2
100-110	6	23.1
110-120	4	15.4
120 plus	6	23.1
	26	100.0

Blood Pressure.—The blood pressure findings did not vary remarkably from normal levels; in fact, the most noteworthy feature is the relatively high level when so much of the literature stresses the state of shock in which the patients are said to be found. The range is demonstrated in Table VII.

TABLE VII

ACUTE PANCREATITIS

BLOOD PRESSURE READING

SYSTOLIC IN MM. HG.	NO. OF PATIENTS	PERCENTAGE
90-100	1	3.8
100-110	1	3.8
110-120	5	19.3
120-130	6	23.1
130-150	8	30.8
150-200	2	7.7
Unrecorded	3	11.5
	26	100.0

Objective Symptoms.—Tenderness was confined to the right hypochondrium in only 6 instances, or 23.1 per cent; while in a series of 301 cases of acute cholecystitis, such a localization was apparent 280 times, or 93 per cent. A more diffuse tenderness which could be localized only

as epigastric was observed 17 times, or in 65.5 per cent of the cases. Tenderness was confined to the left upper quadrant once and, because of the subacute nature of the process and the presence of a palpable mass, a diagnosis of pancreatic cyst was made. In the remaining patient with tenderness restricted to the lower right quadrant, a diagnosis of acute appendicitis was made and the error was not apparent until free blood exuded as the peritoneum was opened via a McBurney incision. One patient in the group flatly denied any tenderness, but at operation there was found marked involvement of the pancreas with a patent foramen of Winslow and a large amount of free blood in the peritoneal cavity. She made a remarkably rapid recovery.

Spasms.—Muscle spasm in any acute intra-abdominal lesion varies with the duration and progress of the disease, so these findings depend largely upon the time after onset that the examination is made.

The extension of muscle spasm from the right hypochondrium to involve the epigastrium and left upper quadrant was noted 12 times, or in 46.3 per cent of the cases. Three of these were described as board-like. Only 5 times was the muscle spasm limited to the right upper quadrant, while in 2 cases it was limited to the left hypochondrium. The 1 case in which other findings were limited to the right lower quadrant also had muscle spasms in this area. In 1 case only was the midepigastrium the sole site of muscle spasm. Five times the examiner reported muscle spasm as entirely absent. All of these, however, had definite tenderness and elevated white counts. It is of special interest that the first time Cullen's sign was observed in a case of pancreatitis in this clinic, muscle spasm was entirely absent. The process in this case was of the fulminating type and the patient expired thirty-six hours postoperatively.

Shock.—Apparent shock was commented on in the records of 4 cases. An analysis of these records for true evidence of shock revealed it was present in only 2 instances if the pulse, temperature, and blood pressure changes are the criteria. Koster and Kasman report shock 7 times in 22 cases with a systolic blood pressure below 90 in 3 of them. Our somewhat larger series shows only one instance of a systolic pressure below 100.

Palpable Mass.—A definitely palpable mass was found 4 times, an incidence of 15.4 per cent. In all of these the process was still definitely acute.

Cullen's Sign.—Cullen's sign, the value of which has been reported in a previous communication, was noted 3 times, for an incidence of 11.5 per cent.

Cyanosis.—Cyanosis was observed and recorded only twice. A note as to its absence was found 6 times and in the remainder no mention

of it was made. The rate of respiration recorded in Table VIII coincides with such a lack of cyanosis; this is in definite contrast to the classical descriptions.

TABLE VIII

ACUTE PANCREATITIS

RESPIRATORY RATE

RATE PER MIN.	NO. OF PATIENTS	PERCENTAGE
16-24	16	61.6 (normal)
25-32	7	26.9 } 38.4% abnormal
33-40	3	11.5 }
	26	100.0

Jaundice.—Jaundice was observed and noted in about one-fourth of the cases; namely, 6 times, or 23.1 per cent. This is in accord with the 4 observations of jaundice in the 22 cases reported by Koster and Kasman.

Distention.—Distention was recorded as marked in only 2 cases.

LABORATORY FINDINGS

Leucocytosis.—The most consistent laboratory finding was an elevated white blood count. The variation, however, was extreme, ranging from 8,550 in a case with marked hemorrhage into the transverse mesocolon and a large amount of free blood in the peritoneal cavity to 45,000 in another case with free blood and fat necrosis. Both patients recovered after long hospitalization.

The variation of the white count is demonstrated in Table IX. The largest number falls in the 20,000 to 30,000 bracket and the average count was found to be 21,000, which is somewhat higher than usually found in the reported cases available for study.

TABLE IX

ACUTE PANCREATITIS

LEUCOCYTOSIS

WBC PER CU. MM.	NO. OF PATIENTS	PERCENTAGE
8,000-10,000	1	3.8
10,000-12,000	1	3.8
12,000-15,000	4	15.4
15,000-20,000	8	30.8
20,000-30,000	9	34.7
30,000-45,000	3	11.5
	26	100.0

The polymorphonuclear count was recorded 24 times and varied from 83 per cent to 98 per cent. The average count was 88.6 per cent.

Urinalysis.—Urinalysis showed only one consistent feature, a positive test for albumin in 16 cases, an incidence of 61.6 per cent.

Reducing substances were noted only 4 times.

Positive tests for bile in the urine were obtained only 4 times, an incidence of 15.4 per cent.

Icterus Index.—Only 4 readings of the icterus index were recorded, none of which was particularly high. They varied from 10.0 to 14.0 with an average of 12.2.

Blood Sugar.—Observations of the blood sugar were equally disappointing. Only 8 preoperative recordings were found, 3 of which were elevated, varying from 128 to 147 mg. per cent.

Blood Chloride.—Blood chloride determination was done only once. In this case vomiting was a very pronounced feature and the chloride level was 380 mg. per cent. Experimentally Dragstedt found that the disease had little effect on the blood chloride level.

Nonprotein Nitrogen.—Five nonprotein nitrogen determinations were all in the upper limits of normal.

Blood Diastase.—Blood diastase was not determined in any of the earlier cases. In most of the later ones it was done only postoperatively and the results were not particularly abnormal. In 1 case low readings of 6 to 12 units were consistently found. Marked liver damage was thought to account for this. Another frank case of acute hemorrhagic pancreatitis gave several blood diastase readings of 12 to 14 units.

PREOPERATIVE DIAGNOSIS

The majority of patients with acute pancreatitis present clinical features which lead the observer to suspect disease of the biliary tract. On admission to hospital the first examiner recorded his early impression of the condition. Cholecystitis and cholelithiasis headed the list of possibilities in 16 of the 26 cases, or 61.5 per cent of the total. Perforated ulcer was considered on 7 occasions and acute intestinal obstruction in 4 instances. Acute appendicitis and acute diverticulitis were both mentioned twice, while tabetic crisis, angina pectoris, general peritonitis, subphrenic abscess, ureteral calculus, and mesenteric cyst each entered the diagnostic field once. Acute pancreatitis was mentioned as a possibility 10 times.

TABLE X

ACUTE PANCREATITIS

PREOPERATIVE DIAGNOSIS

DIAGNOSIS	NO. OF PATIENTS	PERCENTAGE
Acute pancreatitis	8	30.8
Acute cholecystitis	8	30.8
Perforated peptic ulcer	6	23.2
Diverticulitis	1	3.8
Mesenteric cyst	1	3.8
Appendicitis	1	3.8
Intestinal obstruction	1	3.8
	26	100.0

Table X summarizes the final preoperative diagnoses. A definite diagnosis of acute pancreatitis was made in 8 cases, or 30.8 per cent of the cases. In 1 patient the diagnosis was easy because he had been operated upon before for the same condition. The diagnosis in 3 patients was based on the presence of a bluish discoloration around the umbilicus, the so-called Cullen's sign. In our experience the presence of an upper abdominal mass and a positive Cullen's sign as was found in 2 of our cases provides the only definite diagnostic criteria, for, of the 8 positive diagnoses, only 2 were made without one or the other of these clues.

Anesthesia.—The bearing on mortality of the various anesthetics used is set forth in Table XI without establishing any point of significance. The effect of the anesthetic agent on the gravely ill patient merits more serious consideration than it usually receives. The relative harmlessness of local as compared with general or spinal anesthesia should not be overlooked when dealing with this and other conditions requiring surgical intervention in the poor risk patient.

TABLE XI

ACUTE PANCREATITIS

ANESTHESIA

AGENT	NO. OF PATIENTS	PERCENTAGE	NO. OF DEATHS	MORTALITY PERCENTAGE
Ethylene and ether	18	69.4	7	41.1
Ether alone	3	11.5	3	100.0
Spinal	4	15.4	2	50.0
Local	1	3.7	0	0.0
	26	100.0	12	46.1

Incisions.—The abdominal cavity was opened through a right rectus incision in 17 instances and on 3 occasions a left rectus incision was used. A high midline incision through the linea alba has much to commend it, though it was employed in only 6 of our cases. This latter incision has the great advantage of not opening into any of the fascial compartments so that, if infection or tissue digestion ensues, there is less destruction of those important structures which maintain the integrity of the abdominal wall. This precaution will lessen the incidence of postoperative ventral hernia and will make possible a more effective repair when hernia does develop.

OPERATIVE FINDINGS

Abdominal Fluid.—In 12 patients, or almost one-half of the cases, there was no excess fluid found in the peritoneal cavity. In the remaining 14 patients an abundance of bloodstained fluid was observed. In 12 instances the fluid was described as being stained with fresh blood and in 2 occasions with altered or old blood.

Culture of Abdominal Fluid.—Cultures of the abdominal fluid found at operation were made in only 10 instances and of these 4 were positive and 6 were negative. The organisms recorded were *Streptococcus viridans,* staphylococcus, gram-positive cocci, and nonhemolytic streptococci.

Fat Necrosis.—The liberation and activation of lipase, the fat-splitting ferment of the pancreas, is of frequent occurrence in acute pancreatitis. Certain isolated small areas of fat in the omentum and mesentery are affected. The activated ferment splits fat into fatty acids and glycerin. The latter is absorbed and circulating calcium unites with the fatty acids to form soaps. These areas appear as small yellowish plaques in the omentum and mesentery. Fat necrosis is so characteristic of the disease that a confident diagnosis of acute pancreatitis can be made in its presence; in fact, these areas often provide the first clue to the diagnosis. Fat necrosis was observed in 16, or 61.5 per cent, of our cases. No satisfactory explanation has been submitted as to why necrosis is present in some cases and absent in others or why isolated and not contiguous areas of fat are involved.

Involvement of the Mesocolon.—The potential space existing between the leaves of the mesocolon is continuous with the retroperitoneal space in which the pancreas lies. In view of this anatomic arrangement the infrequency of involvement of the mesocolon in acute pancreatitis is remarkable. A collection of fluid in the mesocolon was found in only 2, or 7.7 per cent, of our patients, and fat necrosis was observed in only 6, or 23.1 per cent, of the cases.

Approach to the Pancreas.—Although the pancreas is an entirely retroperitoneal organ, it may be exposed anteriorly after gaining access to the lesser peritoneal cavity. There are four avenues of approach to this space: (1) through the gastrohepatic omentum, (2) through the gastrocolic omentum, (3) through the transverse mesocolon, and (4) through the foramen of Winslow. The last named route is not often utilized because of its relatively small size and because in acute pancreatitis it is often obliterated by edema or by filmy adhesions. The lesser peritoneal cavity is seldom entered through the transverse mesocolon, because, in the first place, it entails elevating the greater omentum and the transverse mesocolon into the operative field and also because of a hesitancy on the part of the surgeon to adopt any maneuver that might endanger the middle colic artery. The most direct access to the lesser peritoneal cavity and body of the pancreas, with a right rectus or midline incision, is obtained by going through the gastrohepatic omentum, above the lesser curvature of the stomach. However, an equally satisfactory exposure is effected by going through the gastrocolic omentum below the greater curvature of the stomach. The latter route had the preference in our cases as it was chosen twice as many times as the former.

Region of Pancreas Involved.—Table XII shows that the whole of the pancreas was involved in 19, or 73.1 per cent, of the cases and that the process was limited to the head in 5, or 19.2 per cent, and to the tail in 2, or 7.7 per cent.

TABLE XII

ACUTE PANCREATITIS

REGION OF PANCREAS INVOLVED

REGION	NO. OF PATIENTS	PERCENTAGE
Whole pancreas	19	73.1
Head only	5	19.2
Tail	2	7.7
	26	100.0

Gall-Bladder Involvement.—Table XIII illustrates the frequency with which gall-bladder disease and acute pancreatitis coexist. The finding of 73.1 per cent of our patients with pathologic gall bladders serves to emphasize the relationship which has been stressed by all authors on the subject. The gall bladder and pancreas have much in common; their ducts normally enter into the duodenum together, though the exact relationship varies; their blood supply arises from the same source; and their lymphatic vessels have a rich anastomosis. Of the 3 possible routes for spread of infection from the gall bladder to the pancreas, the lymphatic route appears to be the most feasible. Some support of this theory is given by a consideration of the frequency with which mild degrees of chronic pancreatitis are found in cases of cholecystitis and cholangitis.

TABLE XIII

ACUTE PANCREATITIS

GALL-BLADDER INVOLVEMENT

DEGREE	NO. OF PATIENTS	PERCENTAGE
Chronic cholecystitis	15	57.7
Acute cholecystitis	4	15.4
Gall bladder negative	7	26.9
	26	100.0

Biliary calculi were present in the gall bladder in 15, or 80 per cent, of the 19 cases in which the gall bladder was obviously diseased, but were found only twice in the common duct at operation. However, in one patient who expired, autopsy revealed a single small stone plugging the ampulla of Vater. No doubt there were other examples of common duct calculi in the series, for, even under the most favorable conditions, small stones are frequently unrecognized and all the more so when exploration must be hurried because of the condition of the patient. Gallstones, of course, can be a factor in acute pancreatitis only under circumstances in which obturation of the ampulla of Vater permits reflux of bile into the pancreatic ducts. The anatomic variation making

this possible probably occurs in about 60 per cent of cases, as shown by reports fluctuating from 3.5 per cent to 89 per cent.

The question which naturally arises is why is pancreatitis so infrequent if it is caused by spread of infection from the gall bladder either through the lymphatics or by way of the biliary passages? There were 1,716 cholecystectomies performed at the Henry Ford Hospital during the same period the 26 cases of acute pancreatitis of this series were observed. This gives a ratio of 66 to 1, a figure almost identical with that given by Abel who found 30 operations for acute pancreatitis and about 2,000 operations in the biliary tract. Furthermore, if the gall-bladder origin hypothesis is the correct one, acute pancreatitis should be more commonly associated with acute than with chronic cholecystitis and yet Table XIII shows the reverse to be true, for the gall bladder was acutely inflamed in only 15.4 per cent of the cases. Finally, how are we to explain these cases of acute pancreatitis in which the gall bladder shows no evidence of disease? The clinical course of the disease in fulminating cases suggests an overwhelming infection. It may be that a generalized infection becomes localized in the pancreas in the same manner that the lungs bear the brunt of a pneumonic infection.

Operation Performed.—Table XIV summarizes the operations performed on the patients of this series. The best results were obtained in those cases where the operation simply consisted of drainage of the lesser peritoneal cavity. Eleven patients were treated in this manner with 5 deaths, a mortality rate of 27.7 per cent. When cholecystostomy was added, as it was in 13 cases, there were 8 deaths, a mortality rate of 61.8 per cent; and death occurred in 2 of the 4 patients in whom the gall bladder was removed and the common bile duct drained, a mortality of 50 per cent. The finding of a mortality rate of 46.1 per cent, even in such a serious disease as acute pancreatitis, suggests that the method of treatment currently in vogue should be reviewed critically. It has been the procedure in this clinic to operate upon all cases of acute pancreatitis as soon as they are diagnosed or suspected. The fluid balance, of course, is restored and blood transfusions are given to forestall or combat shock. All the patients in the series except the last 3 were treated in this manner.

TABLE XIV

ACUTE PANCREATITIS

OPERATION PERFORMED

OPERATION	NO. OF PATIENTS	PERCENTAGE	NO. OF DEATHS	MORTALITY
Drainage alone	11	42.3	3	27.7
Drainage plus cholecystectomy	2	7.7	1	50.0
Drainage plus cholecystostomy	13	50.0	8	61.8
	26	100.0	12	46.1

It is interesting to conjecture why early authors on the subject felt that it was so necessary to evacuate the products of pancreatic necrosis. Their teaching has been followed by most surgeons in spite of the work of Whipple, who, as long ago as 1913, demonstrated that the peritoneal exudate in acute hemorrhagic pancreatitis was innocuous when injected into the veins and peritoneal cavities of animals. The modern trend is to treat acute pancreatitis conservatively and to operate only when a definite mass appears. The results of drainage of these pseudocysts and abscesses are extremely good and the mortality is low. The proponents of the conservative treatment feel that immediate operation does not benefit the fulminating cases and that the added insult of the anesthetic and the operative trauma may turn the tide against the patient. Their contention receives further support from the conclusions of practically all observers that the outcome of a case depends on the degree of involvement of the pancreas and that this is often determined by the time the patient is seen by the surgeon. Decompression of the biliary system, in our cases at least, did not fulfill the theoretic expectations since the mortality rate in those cases in which cholecystostomy was performed was almost double that of simple drainage of the lesser peritoneal cavity. However, it is conceivable that in the early edematous stage of acute pancreatitis decompression of the biliary system might be of value because there are cases on record in which only edema of the pancreas was found at operation, and yet the patient went on to die of a fulminating pancreatitis. The great drawback of the expectant attitude is in the difficulty of making an accurate preoperative diagnosis. Directly as a result of this study we have treated conservatively our recent cases of acute pancreatitis, including the last three of this series. All of the patients recovered following drainage of abscesses or pseudocysts.

Duration of Operation.—The duration of the operation apparently had little to do with the prognosis, except those lasting an hour and fifteen minutes carried by far the greatest mortality as a consideration of Table XV will indicate.

TABLE XV

ACUTE PANCREATITIS

DURATION OF OPERATION

DURATION OF OPERATION IN HR.	NO. OF OPERATIONS	NO. OF DEATHS	MORTALITY PERCENTAGE
¾	4	2	50.0
1	9	4	44.4
1¼	7	6	85.7
1½	4	0	0.0
1¾	1	0	0.0
2	1	0	0.0
	26	12	46.1

MORTALITY

The duration of the disease prior to operation has received a great deal of attention in recent years. The growing conception is that, if operation is delayed beyond the period of early insult, the prognosis can be improved. Recent authors have gone so far as to recommend absolutely conservative treatment, and, finally, after complete convalescence, elective biliary tract surgery.

In the present series, 22 patients were operated upon during the first week of the disease. The following facts are of interest in their relation to mortality. Seven of these patients were operated upon on the second day. Of these 7, 3 died, 2 in less than 24 hours and the third in 72 hours. This gives a mortality following second-day operations of 42.8 per cent in contrast to a 46.2 per cent mortality in the entire group.

Those operated on the third day did not fare so well in that all three expired in short order, 2 early in the second postoperative day, and the other did not leave the operating room.

The three patients operated upon during the first 24 hours of the disease recovered, while one operated upon on the nineteenth day in a moribund condition lived only 8 hours.

The early days of the disease, after the first 24 hours, appear to be the most dangerous for operation. It is not until the eighth day is reached that a definite drop in mortality is noted.

The most outstanding feature in regard to mortality is the short span of life postoperatively. Twelve deaths occurred in the series, 8 of them within the first two days following operation, an average duration of life of only 21 hours. Two more deaths occurred on the third postoperative day. The question worthy of consideration is whether or not any of

TABLE XVI

ACUTE PANCREATITIS

RELATION OF MORTALITY TO TIME OF OPERATION

DAY OF DISEASE OPERATED UPON	NO. OF OPERATIONS	NO. OF DEATHS	DURATION OF LIFE	MORTALITY RATE
1	3	0	--	--
2	7	3	16 hr. 72 hr. 7 days	42.8
3	3	3	20 hr.	100.0
4	3	2	24 hr.	66.6
5	1	0	--	--
6	3	2	10 hr. 3½ days	66.6
7	2	1	17 days	50.0
8	1	0	--	--
13	1	0	--	--
18	1	0	--	--
19	1	1	8 hr.	100.0

these patients could have tolerated the insult of the pancreatitis had they not been brought to bear the shock of an operation. Many years ago Whipple demonstrated that dogs with experimental pancreatitis had a better chance for recovery if the abdomen was not opened.

Table XVI gives a composite view of the mortality rate and duration of life in relation to the day of disease on which operation was performed.

Hospital Stay.—The period of hospitalization varied from 16 to 96 days. Of the 14 patients who recovered, 9 had an average hospital stay of 19½ days, which is not much longer than the anticipated time for other upper abdominal surgery. In the remaining 5 cases the average period of hospitalization was 60 days.

Recurrences.—Five of the 14 patients who recovered were readmitted with findings which were taken as indication of a recurrence of pancreatitis. Four of them were followed conservatively. The fifth was operated upon and he expired. Necropsy revealed an acute pancreatitis with widespread necrosis.

SUMMARY AND CONCLUSIONS

1. An analysis of 26 cases operated upon for acute pancreatitis at the Henry Ford Hospital is presented.

2. Noteworthy features of the cases were the general mildness of the symptoms and the absence of shock.

3. A correct preoperative diagnosis was made in 30.8 per cent of the cases.

4. All but 3 cases were treated by immediate operation.

5. The mortality rate was 46.1 per cent.

6. With simple drainage of the lesser peritoneal cavity, the mortality was only 27.7 per cent, but, when cholecystostomy was added, the mortality rose to 61.8 per cent.

7. The short duration of life postoperatively in the fatal cases suggests that operation precipitated the fatal outcome.

8. A direct result of this review has been a tendency toward delayed operation.

REFERENCES

1. Abel, Irvin: Acute Pancreatitis, Surg., Gynec. & Obst. **66**: 348-353, 1938.
2. Dragstedt, L. R., Haymond, H. E., and Ellis, J. C.: Pathogenesis of Acute Pancreatitis (Acute Pancreatic Necrosis), Arch. Surg. **28**: 232-291, 1934.
3. Fallis, L. S.: Cullen's Sign in Acute Pancreatitis, Ann. Surg. **106**: 54-57, 1937.
4. Farnam, Louise W.: Pancreatitis Following Mumps: Report of a Case With Operation, Am. J. M. Sc. **163**: 859-870, 1922.
5. Henderson, F. F., and King, E. S. A.: Acute Pancreatitis, Arch. Surg. **30**: 1049-1057, 1935.
6. Koster, H., and Kasman, L. P.: Acute Pancreatitis, Arch. Surg. **29**: 1014-1923, 1934.
7. Mann, F. C., and Giordano, A. S.: The Bile Factor in Pancreatitis, Arch. Surg. **6**: 1-30, 1923.

8. Opie, E. L.: Disease of the Pancreas, Ed. 2, Philadelphia, 1910, J. B. Lippincott Company.
9. Parry, John R., and Murray, Kenneth: Acute Pancreatic Necrosis (A Review of Twenty Cases), Canad. M. A. J. **31**: 592-595, 1934.
10. Trasoff, Abraham, and Scarf, Maxwell: Acute Pancreatitis: A Medical Problem, Am. J. M. Sc. **194**: 470-474, 1937.
11. Wangensteen, O. H., Leven, N. L., and Manson, M. H.: Acute Pancreatitis (Pancreatic Necrosis). An Experimental and Clinical Study With Special Reference to the Significance of the Biliary Tract Factor, Arch. Surg. **23**: 47-73, 1931.
12. Whipple, G. H., and Goodpasture, E. W.: Acute Haemorrhagic Pancreatitis, Surg., Gynec. & Obst. **17**: 541-547, 1913.
13. Wildegans, H.: Abwartende oder primär chirurgische Behandlung der akuten Pancreasnekrose? Der Chirurg. **8**: 597-604, 1936; Int. Surg. Dig. **22**: 262-264, 1936.

ACUTE SUPPURATIVE APPENDICITIS COMPLICATING SEVERE UNTREATED THYROTOXICOSIS

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THE occurrence of acute abdominal crises in such intoxications and metabolic disturbances as plumbism and diabetes mellitus, although infrequent, is quite well known. Of greater rarity is the occurrence of acute abdominal pain in thyrotoxicosis. A few cases have been reported by Stern,[1] Kraus,[2] Horsley and Rosebro,[3] and Desbouis.[4] More recently Robertson and his associates[5] have dealt with this problem. They reported three cases of "hyperthyroidism masked by symptoms of acute abdominal catastrophe," and in one case the abdominal symptoms so closely mimicked acute appendicitis as to cause a surgical consultant to remove the appendix, which proved to be normal. On the other hand, failure to recognize a true acute intra-abdominal lesion requiring immediate surgical intervention may be disastrous. The difficulties in differential diagnosis are obvious and require no further comment.

In a consecutive series of over 2,000 patients requiring thyroidectomy for thyrotoxicosis, Richter[6] has had occasion but twice to perform laparotomy for acute intra-abdominal disease. Interestingly enough, in both patients the operation was undertaken for acute suppurative cholecystitis. In these two instances the patients were under treatment for thyrotoxicosis (receiving Lugol's solution in adequate dosage) which minimized the danger of postoperative reaction. In the case to be presented, a somewhat different problem was encountered. Here we had to deal with a patient who had an acute suppurative intra-abdominal lesion, but who also presented most marked symptoms of high grade hyperthyroidism for which she had never been treated. One needs but to recall the high mortality and morbidity associated with operations on the thyroid gland (for thyrotoxicosis) in the preiodine era, as well as the occurrence of thyroid crisis following apparently trivial surgical procedures (as incision of a furuncle or infection of a varicose vein[7]) to understand the surgical problem encountered in this patient. The salient facts are herewith presented.

REPORT OF CASE

I. B., a 23-year-old white girl, first came under observation in October, 1934, complaining of palpitation, heat intolerance, and nervousness. She had been perfectly well until that time. The past history was without significance; the menses began at 13 years of age, and were of the regular 30-day type, duration 5 days.

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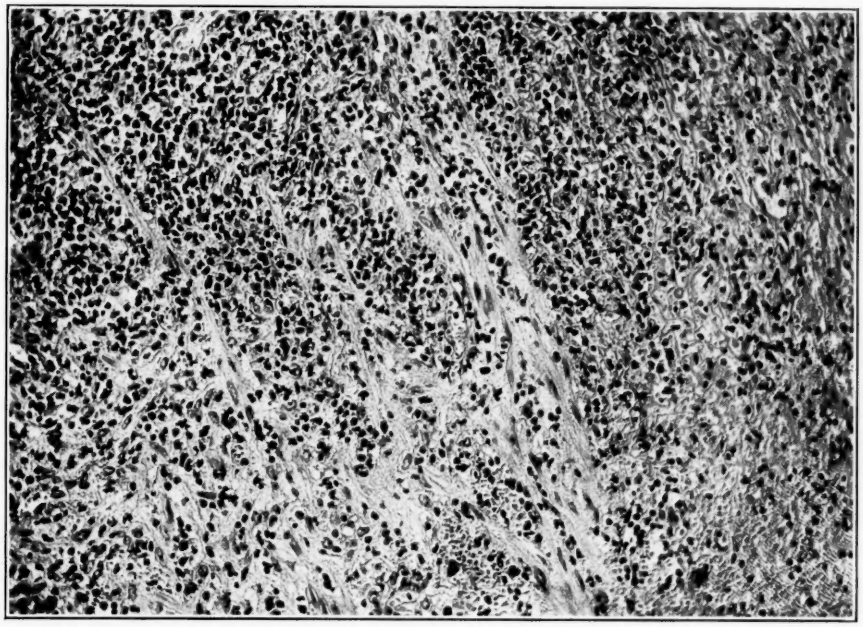

Fig. 1.—Wall of appendix, showing destruction of normal architecture, diffuse infiltration with eosinophilic and neutrophilic leucocytes, and deposits of fibrin (low power, ×200).

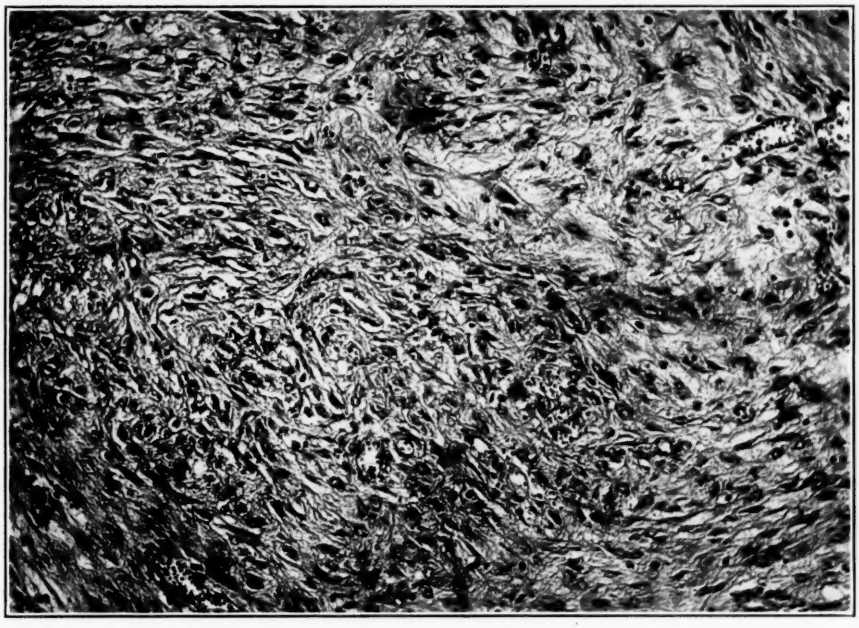

Fig. 2.—Periappendiceal mass. Granulation tissue with large number of fibroblasts and capillaries; infiltration with leucocytes, chiefly neutrophils (low power, ×200).

The essential physical findings at this time consisted of slight, diffuse, symmetrical thyroid enlargement, pulse rate of 92 to 100, tremor of fingers and tongue, systolic blood pressure of 128, and diastolic pressure of 65. Two basal metabolic rate determinations at this time were plus 28 and plus 30. A diagnosis of toxic (diffuse) goiter was made and the patient was advised to have thyroidectomy after proper iodine preparation. This was refused and she was not seen again for over a year, when she again presented herself with the same, but more marked, symptoms. The palpitation was now more persistent; there was slight bilateral equal exophthalmos; weight loss of 12 pounds in the preceding 8 weeks had occurred; the skin was warm and moist, the pulse rate 110 to 120, systolic blood pressure 136 and diastolic pressure 60. The basal metabolic rate was plus 28. She again refused thyroidectomy. She was seen on two occasions in the next eighteen months, and attention was called to the definite progression of symptoms, but all efforts to persuade her to accede to surgical treatment were futile.

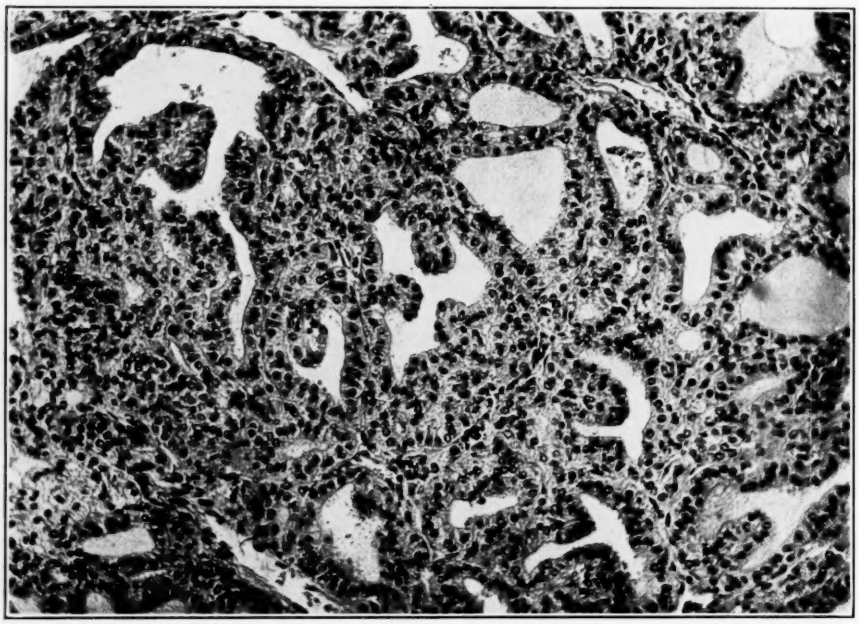

Fig. 3.—Hyperplasia of thyroid. Epithelial cells are high columnar. Many papillary projections are seen. Colloid is thin or absent. (Low power, ×200.)

Such was the state of affairs when on the evening of Aug. 4, 1937, she was seized with severe generalized abdominal pain. She became nauseated, felt "feverish," but did not vomit. The pain became cramplike, and the next morning was most marked in the right lower abdominal quadrant. She vomited three times on the following day. There were no urinary disturbances, no diarrhea, and no symptoms referable to the respiratory tract. She was seen by us on Aug. 6, 1937, some forty hours following the onset of abdominal pain. Her appearance was that of a seriously sick patient. She was restless, irritable, and tremulous; the cheeks were flushed, and the skin, warm and moist. The temperature was 103° F. (rectally), the pulse rate 160, and the blood pressure 150/70. There was moderate bilateral equal exophthalmos, tremor of tongue, diffuse symmetrical enlargement of the thyroid, and tremor of the outstretched fingers. There were no cardiac abnormalities, save for the tachycardia and a soft systolic apical murmur which was not transmitted.

Abdominal examination disclosed diffuse tenderness, most marked in the right lower quadrant over the appendiceal area, right rectus rigidity, marked rebound tenderness, and a positive Rovsing sign. On rectal bimanual examination (the hymen was intact), there was tenderness high up on the right side. The leucocyte count was 18,300, with 78 per cent polynuclears; there were no urinary abnormalities. The diagnosis made was acute suppurative appendicitis and severe hyperthyroidism, and the patient was immediately hospitalized.

Realizing the grave danger of laparotomy in the presence of severe thyrotoxicosis, it was thought best to defer operation for some eight to ten hours, during which time we could institute measures to lessen the risk of crisis. Accordingly, she received 4,500 c.c. of normal saline solution with dextrose (5 per cent) intravenously, and sodium iodide, 75 gr. (5.0 gm.) by the same route in divided doses. Morphine sulfate was administered twice in quarter grain doses during this interval.

The pulse rate remained at 160 per minute, but the patient felt less nervous, irritable and restless.

Operation and Clinical Course.—Operation was performed on Aug. 6, 1937, some forty-eight hours following the onset of the abdominal pain. Under nitrous oxide-oxygen anesthesia with infiltration of the abdominal wall with 0.5 per cent novocain solution, the abdomen was opened through a muscle-splitting incision. A small amount of free turbid peritoneal fluid escaped and a large acutely inflamed mass was encountered, consisting of the appendix and an adherent tumor lying in a small pool of pus. The entire mass was quickly delivered and removed without inverting the appendical stump, and the abdomen closed without drainage. (The gross appearance of the removed tumefaction was that of an acutely inflamed appendix with a granuloma or carcinoid tumor.) During the operation the pulse rate varied from 160 to 180 per minute, and the systolic blood pressure readings fluctuated from 140 to 168, the diastolic level remaining at 80.

The immediate postoperative treatment consisted of continuation of the phleboclysis with saline solution and dextrose (5 per cent) and Lugol's solution equivalent to 120 minims during the first 24 hours, 60 minims daily for the next three days, and 45 minims daily thereafter. Morphine and phenobarbital were used liberally for sedation. The first five postoperative days were stormy; the temperature ranged from 101° F. to 104° F.; the pulse rate varied from 120 to 180 per minute and the patient was restless and extremely irritable, although as cooperative as circumstances permitted. The temperature gradually declined and the pulse rate diminished, the former reaching normal on the ninth postoperative day. Convalescence thereafter was smooth, being marred only by a mild wound infection which yielded readily to Dakinization. She was discharged on the twenty-first postoperative day, with the wound healed, and advised to return in three weeks for thyroidectomy. The basal metabolic rate on discharge was plus 26.

Second Operation.—The patient returned for thyroidectomy three weeks after discharge from the hospital, having been on Lugol's solution, 45 minims daily, during the interval. She had gained seven pounds and had improved remarkably. The preoperative basal rate was plus 15. Subtotal thyroidectomy was performed under nitrous oxide-oxygen anesthesia with infiltration of the skin and muscles with 0.5 per cent novocain solution. A large symmetrical hyperplastic gland was removed. Recovery was uneventful and she was discharged on the seventh postoperative day, with a basal metabolic rate of plus 10. She has remained well since discharge following the thyroidectomy.

Pathologic Report.—(Dr. I. Davidsohn.) Acute suppurative appendicitis and periappendicitis; granuloma; hyperplastic goiter.

SUMMARY

A case of acute suppurative appendicitis is reported, which occurred in the course of a severe untreated thyrotoxicosis. Appendectomy was successfully carried out following an eight-hour preparation with large doses of iodine intravenously, phleboclysis, and sedation with morphine. Thyroidectomy was performed later without incident.

Attention is directed to the rarity of acute abdominal pain occurring in thyrotoxicosis, the difficulty in differentiating the pain due to organic intra-abdominal disease requiring surgical intervention from the abdominal pain which may be due to the underlying intoxication, and the grave danger of operating upon thyrotoxic patients improperly prepared.

REFERENCES

1. Stern, R.: Differential diagnose und Verlauf des Morbus Basedowii und seiner unvollkommenen Formen, Vienna, 1909, Franz Deuticke.
2. Kraus, Carl: Zur Klinik des Morbus Basedowii und seines Grenzgebietes, Med. Klin. **1**: 171, 1911.
3. Horsley, J. S., and Rosebro, B. M.: An Atypical Case of Hyperthyroidism, New York M. J. **95**: 267, 1912.
4. Desbouis, G.: Crises Enteralgique au cours d'une maladie de Basedow, Bull. et mem. Soc. med. d. hôp. de Paris **37**: 811, 1914.
5. Robertson, W. E., Wohl, M. G., and Robertson, H. F.: Hyperthyroidism Masked by Symptoms of Acute Abdominal Catastrophe, J. A. M. A. **108**: 623, 1937.
6. Richter, H. M.: Personal communication.
7. Greene, E. I., and Greene, J. M.: Fatal Thyroid Crisis Following Injection of a Varicose Vein, J. A. M. A. **96**: 611, 1931.

LEFT RETROMESOCOLIC HERNIA

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IN A PREVIOUS communication[1] I presented a case of right retromesocolic hernia. At that time there were on record forty-nine authentic cases of this kind of hernia. Since then two others have been added, one by Paul and Hill[2] and another by Baumeister and Hanchett.[3] Recently it was my good fortune to encounter a case of left retromesocolic hernia, a condition first described in detail by Treitz (1857) and since then called the hernia of Treitz. According to the figures given by Moynihan,[4] Andrews,[5] and Longacre,[6] left retromesocolic hernia seems to occur about three times more frequently than the right. In most of the recorded instances, as in that of Callander, Rusk, and Nemir,[7] and that of Emenhiser and Pankratz,[8] the hernial sac contained all of the jejunum and almost all of the ileum. In the case herein described, only a portion of the jejunum was enclosed in the hernial sac and the peritoneal and vascular relations were thus well enough preserved to illuminate the mechanism producing this condition.

CASE REPORT

S. B., a 55-year-old colored man, was admitted to the Charity Hospital of Louisiana at New Orleans, Aug. 25, 1938, in a state of unconsciousness. According to a friend, he had been a heavy drinker for two years and on the day before admission he was found naked and unconscious, with short, stertorous breathing, and was bathed in sweat. His blood pressure was unobtainable; the pulse rate was 100 per minute; the respirations, 28; and the rectal temperature, 102° F. The cardiac impulse was not seen or felt, the heart tones were of poor quality, and the rate and rhythm were regular. Large, moist râles were heard over both lungs. The urine was bloody. Supportive treatment was of no avail. On the following day the patient's temperature rose to 104° F. and he died at 11:05 A.M., about fifteen hours after admission.

The necropsy (A-38-862) revealed bronchitis, bronchiolitis, and lobular pneumonia, an enlarged prostate, hypertrophy of the urinary bladder with diverticula and acute cystitis, slight cirrhosis of the liver, a small accessory spleen, and an intraperitoneal hernia. The latter was of particular interest.

The peritoneal cavity contained no excess fluid and its surfaces were smooth and glistening. No changes were noted in the disposition of the upper abdominal organs. Below the transverse mesocolon, on the left side of the vertebral column, there was a peritoneal pocket, 12 by 12 cm., with an oval opening to the right 8 by 7 cm. Near the free margin of the peritoneal fold bordering the opening ran the inferior mesenteric vein and the ascending branch of the left colic artery.

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The pocket, situated in the region of the duodenojejunal fossa, contained the left inframesocolic portion of the duodenum and about 90 cm. of jejunum. The loops of jejunum were easily removed, since they were practically empty and there were no adhesions between the loops or the pocket. The rest of the jejunum and the ileum was collapsed and empty. The appendix was in a medial position and 6 cm. long. The position of the cecum, colon, and rectum was as usual.

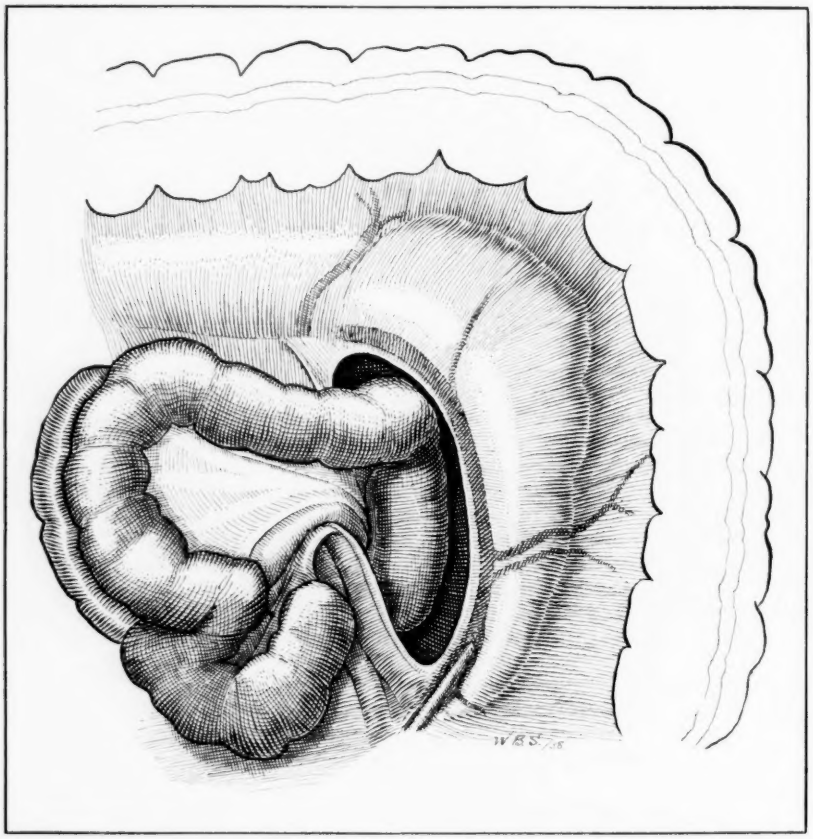

Fig. 1.—Below the transverse mesocolon, in the region of the duodenojejunal fossa, there is a peritoneal pocket which contains the left inframesocolic portion of the duodenum and from which 90 cm. of jejunum have been removed. The anterior wall of the pocket containing the inferior mesenteric vein and the left colic artery in their usual relation is a part of the descending mesocolon, hence the name *hernia retromesocolica sinistra.*

COMMENT

This hernia, like the type which occurs on the right side, is to be interpreted as a malposition of the part of the small intestine involved, rather than as a herniation into a preformed peritoneal sac. This malposition is due to a faulty orientation of the developing gut during that period of its rotation when the cecum migrates toward the right iliac fossa and the descending mesocolon becomes fused with the parietal peritoneum. The failure of the craniomedial half of the descending mesocolon to fuse with the parietal peritoneum leaves a pocket enclosing a part of the duodenum (the left inframesocolic portion) and some loops of the

proximal jejunum. This pocket, which forms the hernial sac, opens toward the right. Its anterior wall, which contains the inferior mesenteric vein and the left colic artery in their usual relation, is a part of the descending mesocolon, hence the name *hernia retromesocolica sinistra.*

SUMMARY

Malposition of a part of the small intestine in a peritoneal sac behind the descending mesocolon is described and interpreted as a left retromesocolic hernia. This type of hernia is about three times more frequent than that occurring on the right side.

REFERENCES

1. Halpert, Béla: Right Retromesocolic Hernia, SURGERY **3:** 579, 1938.
2. Paul, Milroy, and Hill, Osman: Right "Duodenal" Hernia, Brit. J. Surg. **25:** 496, 1938.
3. Baumeister, Carl, and Hanchett, McMicken: Right Paraduodenal Hernia, Arch. Surg. **37:** 327, 1938.
4. Moynihan, B. G. A.: On Retro-Peritoneal Hernia, New York, 1906, William Wood & Company.
5. Andrews, Edmund: Duodenal Hernia—A Misnomer, Surg., Gynec. & Obst. **37:** 740, 1923.
6. Longacre, J. J.: Mesentericoparietal Hernia. Duodenal Hernia of Treitz, Surg., Gynec. & Obst. **59:** 165, 1934.
7. Callander, C. Latimer, Rusk, Glanville Y., and Nemir, Alma: Mechanism, Symptoms and Treatment of Hernia into the Descending Mesocolon (Left Duodenal Hernia), Surg., Gynec. & Obst. **60:** 1052, 1935.
8. Emenhiser, Lee K., and Pankratz, David: Left Intraperitoneal Hernia, Am. J. Surg. **34:** 104, 1936.

HERNIA THROUGH THE BROAD LIGAMENT

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(From "The Clinic")

ONLY sixteen cases of true hernia into or through the broad ligament have been reported to date. All of these, save one, have been of the intestinal type. In this single case, reported by Masson and Atkinson, the hernial sac contained a Fallopian tube and ovary. The first authentic case of broad ligament hernia was that described by Quain in 1861. He performed an autopsy on a 36-year-old multipara who had died, without operation, following an incarceration of small intestine through an opening in the right broad ligament. There is a long hiatus in the literature until 1917, when Fagge reported two cases of intestinal hernia through the broad ligament. Since that time, the following additional cases have been reported: 1920, Barr (1), Richardson (1); 1924, Pidcock (1); 1926, Dunn (1); 1928, Dorman (1), Stimson (1); 1929, Pemberton and Sager (1), Janes (2); 1930, Coplan (1); 1931, Cooper (1); 1933, Masson and Atkinson (1); 1934, Hunt (1). Total cases to date, 16.

Of this number, only two have followed the Baldy-Webster operation for uterine suspension. These were the cases of Richardson and Pemberton and Sager. Strangulated hernias through the broad ligament were found in both of these patients at two years and ten days, respectively, following the uterine suspensions. Our first case, an account of which will follow, is the third case to be reported of broad ligament hernia following the Baldy-Webster uterine suspension.

The youngest case of the series was reported by Hunt. The patient was 25 years old and the hernia was incidentally discovered when she was being delivered of her third child by low cervical cesarean section. Undoubtedly as our attention is drawn to this condition more cases will be reported. The oldest in the series was Cooper's case, aged 70 years. The patients were almost exclusively multiparous, most of them having borne three or more children. Two were nulliparas, aged 49 and 30 years. The average age incidence for 15 of the 16 cases was 49 years; Dorman did not give the age of his patient. Of the total series of 16, 6 of the hernias occurred on the right, while 10 involved the left broad ligament. No case has yet been reported in which a hernia has been present on both sides simultaneously. Dunn's case, however, had a large window through the broad ligament opposite the site of the broad ligament hernia. The cecum and appendix were adherent to the edge of the

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ring and it is quite conceivable that, had there been a mobile cecum, this could easily have passed through so large an aperture as was present in the right broad ligament.

ETIOLOGY

As usual we must consider predisposing and exciting causes. Developmental anomalies, such as pouches, fenestrations, or mere anatomic weakness in the intrinsic structure of the broad ligament must be mentioned. As a rule textbooks make but scant mention of the embryology of the broad ligaments, but Kostanecki has brought out the fact that, even in the adult normal broad ligament, a degree of weakness persists along the lines of fusion between the medial and lateral parts of the Wolffian mesentery and the phrenicomesonephric ligament. Given the predisposing congenital weakness of this structure plus the necessary force, a hernia may result by the wedging and dissecting action of the viscus which is being thrust in the direction of least resistance. In the series of 5 broad ligament hernias collected by Dunn, all of the hernias entered the openings from above and behind. As Dunn points out, this is the plane which the broad ligaments present to the intestines and which bears the brunt of intra-abdominal pressure. In Richardson's case and in our first case, both of which followed the Baldy-Webster uterine suspension, the gut passed through the hernial opening from before backward. In Pemberton and Sager's case, however, after the same type of operation, the gut passed through the hole in the reverse direction.

Multiparity and middle age with their relaxations of tissues are further important predisposing causes. The Baldy-Webster operation in which a hole is torn through the broad ligament on each side and through which the relaxed round ligament is pulled to be sutured to its fellow on the posterior surface of the uterus is a very important potential source of trouble. In Richardson's case the Baldy operation had been performed two years previously without suture of the openings through the broad ligaments as urged by the originators of the operation. He found three or four inches of gut strangulated in the opening in the right broad ligament. Pemberton and Sager report another such occurrence in a patient ten days after the Baldy-Webster operation. In this case both openings in the broad ligament had been closed according to the original technique. They also reported a second patient who was operated on for large uterine myomas. She had had a Baldy-Webster suspension operation twelve years previously. At hysterectomy the operators made the incidental findings of a large opening in each broad ligament where the tunnels had been placed for the round ligaments. The openings, however, contained no viscera. Hence, whether the openings through the broad ligaments are sutured according to the original technique or not, one cannot be entirely safe. It

would seem that, if the Baldy-Webster operation is ever performed, these openings should be firmly sutured with nonabsorbable material. The herniation may take place a few days or many years after the Baldy operation. Among the exciting causes of broad ligament hernia should be mentioned falls, straining at stool, or during childbirth, or any violence whereby a viscus could be thrust through an already weakened tissue. Not infrequently there is no tangible exciting cause. In the case of the larger openings it is quite conceivable that a loop of gut may be present in a hernial pouch or may even be thrust for a considerable distance through an aperture without detection until at some future date the crisis is precipitated and the true condition discovered. As Hunt has brought out, the broad ligament is divided into two triangular areas; the smaller portion is uppermost and is separated topographically from the lower and larger triangle by the ligamentum proprium ovarii. The hernias may pass through either of the triangles.

DIAGNOSIS

There are no infallible diagnostic criteria. Hernias through the broad ligament present the same variations and vagaries of symptomatology that are seen in other types of acute intestinal obstruction and are subject to the same delays in therapy. Any patient who has had a Baldy-Webster operation, no matter how many years previously, and who develops sudden acute obstructive symptoms referable to the intestinal tract may have a broad ligament hernia. Unfortunately tenderness in the cul-de-sac or in the region of the adnexa or the presence of a palpable tender mass in these areas is not of much help. It is quite possible to have a broad ligament hernia with no symptoms nor findings suggesting trouble within the pelvis.

TREATMENT AND PROGNOSIS

The treatment is operative and should be carried out immediately or temporarily deferred according to whether the patient's condition will permit or whether time must be taken to replace lost fluids and blood chlorides. The earlier the operation, the better the prognosis. Those who are operated upon too late will die, just as will those patients with acute ileus due to any other cause. In the series of 16 cases of hernia through the broad ligament, 15 were operated upon. Quain's case in 1861 was examined only at autopsy without having been operated on. Eleven recovered, 3 with stormy convalescences due to complications. Janes' second patient, who was suffering from auricular fibrillation at the time of operation, died seventeen hours after laparotomy. Stimson's case was hopelessly ill from a four-day bowel blockage and died shortly after the peritoneum was opened. Most of the cases received general anesthesia, but we favor the use of spinal anesthesia whenever possible for reasons which must be obvious without detailed argument.

In some cases the fenestrae or pouches in the broad ligament may be closed by suturing. At other times the offending area is removed by salpingo-oophorectomy. Again it may occasionally suffice to simply incise the roof of the tunnel through the broad ligament, as we did in our case, peritonizing the raw edges as they retract in order to eliminate re-formation of the aperture.

ADDITIONAL CASE REPORT

CASE 17.—Aged 42 years, Caucasian-Hawaiian, gravida iii, para ii. She was brought to our office in a state of collapse, Feb. 25, 1938, at noon. She had been teaching school as usual from early in the morning. Forty-five minutes before we saw her she was seized as she stood by an agonizing pain low in the left pelvis. She fainted and felt very weak when she regained consciousness. She was nauseated but did not vomit at the time. Generalized pallor was noted and the entire body was bathed in clammy sweat. Blood pressure was 120/68. Abdomen flabby with old healed striae gravidarum; no distention; no rigidity but generalized moderate degree of tenderness noted. Usual tinkling type of peristalsis heard throughout abdomen. On pelvic examination uterus approximately normal size but very hard with a smooth round walnut-sized knob palpable on its upper left anterior surface. No cul-de-sac or adnexal masses or tenderness was noted. Knee jerks slightly accentuated. Hemoglobin (Newcomer), 48 per cent; red blood count, 2,500,000. Urine normal except for a very faint trace of albumin. She was admitted at once by ambulance to Queen's Hospital where efforts were directed toward combating shock. It was felt that immediate laparotomy was inadvisable. She was given 500 c.c. of citrated whole blood intravenously shortly after her admission with noticeable improvement. In addition Hartmann's solution was given in liberal quantities intravenously. As she improved, a more coherent history was obtained from her. She had been in excellent health until after her children were born. These were born normally twenty and sixteen years previously. Following that she induced a miscarriage nine years ago at five and one-half months. Menstrual history: Onset at 12 years of age, irregular until marriage. Occasional slight dysmenorrhea. Sixteen years ago she had had a Baldy-Webster operation done for retroversion of the uterus. On Dec. 31, 1937, she consulted us regarding profuse vaginal bleeding recurring two or three times a month and lasting for as long as seven successive days. An irregular hard knobby uterus was clearly felt. Operation was advised, but this was declined. She received radium therapy elsewhere. The bleeding ceased, and the uterus decreased perceptibly in size. A definite anemia persisted, however. The patient continued with her work as a primary school teacher until she collapsed with abdominal pain. During the twenty-four hours which elapsed after her admission, her general condition improved markedly, but unmistakable signs of bowel obstruction developed. Laparotomy was performed thirty-six hours after the onset of the pain. The preoperative diagnosis was acute intestinal obstruction.

After the first blood transfusion of 500 c.c. the hemoglobin was 52 per cent; red blood count, 3,580,000; white blood count, 15,750 with 96 per cent neutrophiles. A second transfusion of 550 c.c. of citrated whole blood was commenced at the beginning of the operation. Intrathecal anesthesia was used, giving 110 mg. of neocain to which was added 0.75 c.c. of pantocain.

Midline incision; numerous adhesions of omentum to the parietal peritoneum were seen. Several had to be freed before adequate exposure of viscera was obtained. Many coils of atonic, but otherwise good-looking, small gut were first

examined, after which the main mass of intestines was displaced cephalad by hot gauze packs. Approximately 750 c.c. of clear straw-colored fluid was aspirated from the pelvic cavity. No pus or free blood was encountered. A boggy, dark, beefy red loop of ileum 20 inches long was found doubled tightly on itself and bulging or rather herniating through an opening 2 cm. in diameter just below the right ovarian ligament as shown in Fig. 1. The gut apparently had entered the opening in an anteroposterior direction as shown. No attempt was made to pull the gut through the hole as it was obviously impossible due to edema. The roof of the tunnel consisted of the right ovarian ligament, mesial portion of right tube, and remnants of the right round ligament (mostly scar tissue replacement after Baldy type suspension). This roof was laid wide open with blunt-ended scissors, and raw ends were ligated and then oversewn with redundant peritoneum. No attempt was made to remove the distal portion of the right tube nor the right ovary. The released loop of gut was watched for a few minutes and regained much of its natural color. It was considered viable and was left alone. The uterus was seen to contain at least one and possibly more fibroids (Fig. 1). Nothing was done to the fibroids. Uterine attachments of both round ligaments were seen to be on the posterior surface of the uterus. They consisted at these areas of anchorage, of fibrous tissue, and had lost all resemblance to the original tissues. The left Baldy-Webster opening in the broad ligament was apparently closed. The abdomen was closed in layers without drainage.

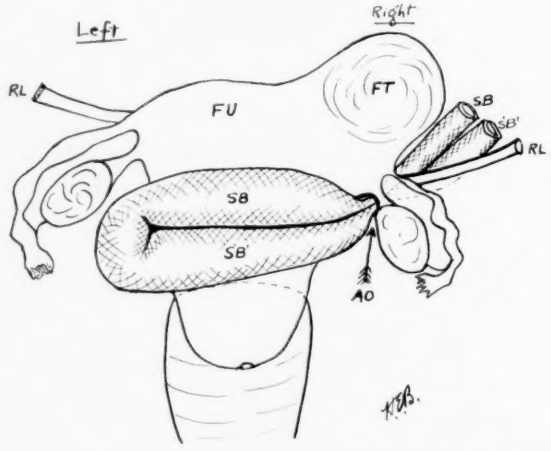

Fig. 1.—Case 17. *RL*, Round ligaments; *FU*, fundus uteri; *FT*, fibroid tumor; *SB*, *S'B'*, small bowel; *AO*, abnormal opening in broad ligament.

The patient tolerated the operation quite well, her condition being definitely better at the end of the procedure than at the beginning. Prior to incision, temperature was 100°; respiration, 22; pulse, 110 (thready). Lowest pressure reading was 80/30. After 1 c.c. of ephedrine by hypodermic, it rose to 126/80 and remained nearly at this figure until the end of the operation. Pulse at close of operation was 130 but regular and strong.

Convalescence was uneventful and she left the hospital on the seventeenth post-operative day in good condition. She has received subsequent intensive treatment for her anemia and is at present well and strong, working full time at her occupation of teaching school.

CASE 18.—Aged 62 years, Caucasian, para iv. Admitted March 1, 1931, to the Kahuku Plantation Hospital near Honolulu with the chief complaint of constipation and vomiting. For eight years she had been troubled with stubborn constipation,

accompanied frequently by severe pain in the left lower abdomen. During the week prior to her hospital admission, the bowels had moved normally. There followed a period of four days with no movement. She attempted catharsis but vomited the epsom salts as soon as they had been swallowed. That night she took an enema with good results and felt all right again until the night before admittance when she again vomited. Another enema following this gave good results.

She had never had any abdominal operations. She had had three cerebral accidents during the past few years, each one paralyzing her for a number of weeks, but apparently leaving no further residua. Persistent hypertension had been present for years. On examination the patient was noted to be quite obese and the heart was markedly enlarged to the left. Blood pressure was 192/90. There was a moderate systolic murmur and an occasional dropped heart beat. The abdomen was moderately distended, but no tenderness, masses, or rigidity was noted. Pelvic findings were negative. The white blood cell count was 6,700. The urine contained considerable albumin but no casts and was otherwise negative. An x-ray photograph of the abdomen showed stepladder fluid levels suggesting intestinal obstruction. The preoperative diagnosis was "partial intestinal obstruction probably due to malignancy with carditis and hypertension."

The patient was operated upon by Dr. H. T. Rothwell and Dr. J. E. Strode, by whose kind permission the case is here reported. A left rectus incision was made under drop ether anesthesia. Spinocain was first given intrathecally but was ineffective. A 4-inch loop of small intestine was found herniated through a congenital foramen in the left broad ligament. The gut had passed through the broad ligament from behind forward. The gut appeared viable and was pulled gently through the foramen, after which the aperture was closed by bringing its edges together. The patient died of cardiac decompensation thirty-six hours after operation.

SUMMARY AND CONCLUSIONS

Broad ligament hernia is one of the rarest of the internal hernias. Only 16 cases have been recorded in the literature to date. Two other cases are presented herewith for addition to the list. The leading predisposing causes of the condition are multiparity, the presence of congenital fenestrae or pouches in the broad ligament, or a preceding Baldy-Webster uterine suspension. Diagnosis is based on the symptoms and signs of intestinal obstruction.

REFERENCES

Barr, H. A.: Strangulated Hernia of the Small Intestine Through the Left Broad Ligament, South Texas M. Rec. **15**: 5, 1920.

Cooper, R. W.: Strangulation of the Small Intestine, Australian & New Zealand J. Surg. **1**: 325, 1931.

Coplan, S.: Strangulated Hernia of Broad Ligament, Brit. M. J. **1**: 950, 1930.

Dorman, W. E.: Hernia Into the Broad Ligament, Brit. M. J. **2**: 528, 1928.

Dunn, L.: Hernia in Broad Ligament From Clinical Point of View, Surg., Gynec. & Obst. **42**: 398, 1926.

Fagge, C. H.: Two Cases of Strangulated Retroperitoneal Hernia Into Pouches of the Broad Ligament, Brit. J. Surg. **5**: 694, 1918.

Hunt, A. B.: Fenestrae and Pouches in Broad Ligament as Actual and Potential Cause of Strangulated Intraabdominal Hernia; Report of 2 Cases Without Strangulation, With Review of Literature, Surg., Gynec. & Obst. **58**: 909, 1934.

Janes, R.: Two Cases of Intestinal Obstruction Due to Strangulation of a Loop of Small Intestine Into an Opening of the Left Broad Ligament, Brit. J. Surg. **17**: 333, 1929.

Kostanecki, K.: L'Evolution de segment lateral du ligament large, J. d'anat., d'histol, et d'embryol. **11-12**: 77, 1930.

Masson, J. C., and Atkinson, W.: Hernias Into Broad Ligament, Proc. Staff Meet. Mayo Clin. **8**: 293, 1933.

Pemberton, J., and Sager, W.: Intestinal Obstruction Following the Webster-Baldy Operation for Retroversion, S. Clin. North America **9**: 203, 1929.

Pidcock, B. H.: Intestinal Obstruction, Brit. M. J. **1**: 369, 1924.

Quain: Case of Internal Strangulation of a Large Portion of the Ileum, Tr. Path. Soc., Lond. **12**: 103, 1861.

Richardson, E. P.: Intestinal Obstruction Following Baldy-Webster Operation for Retroversion: Report of Case, Surg., Gynec. & Obst. **31**: 90, 1920.

Stimson, C. M.: Hernia Strangulated Through the Broad Ligament, Am. J. Obst. & Gynec. **15**: 251, 1928.

PARADUODENAL HERNIA

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A SURGEON is due many surprises in abdominal exploration, but none is more startling than to open an abdomen for intestinal obstruction and find no intestine presenting within the abdominal cavity. Such a picture may be seen with acute obstruction of a paraduodenal hernia. All of the small intestines are contained within a retroperitoneal sac and, as the colon may be crowded entirely outside of the operative field, nothing but a smooth peritoneal covered mass can be seen by the operator. In the case which I will report, the only structure to be felt or seen was a smooth cystlike mass which completely filled the abdominal cavity. The rarity of the condition and the necessity of promptly recognizing its nature in order to meet the situation adequately have prompted reporting this single case.

Case Report.—Mr. C., aged 51 years, first entered the Tuberculosis Pavilion March 2, 1938. In 1916 he had been diagnosed as tuberculous and was sent West where he lived for three years with apparent arrest of the process. He had a recurrence in 1930, at which time moderately far advanced pulmonary tuberculosis involving the entire left lung, with cavitation, was diagnosed. He was treated by pneumothorax and general measures during the following seven years; at one time he developed an effusion, but generally he was in a fair state of health. A recurrence of pulmonary activity with bloody sputum finally brought him to the hospital. He had lost 22 pounds in weight and was quite weak. Subsequent information obtained from his wife showed that for the past four years he had suffered from abdominal colic after meals. The attacks were severe, most often occurring at night. He found relief in the knee-chest position or from local heat applied to the abdomen, and by enemas. As soon as he felt a rumbling in the abdomen and was able to pass gas he was relieved. He found that mineral oil lessened the frequency of the attacks. He was never seen in an attack by a physician as home remedies had been effective.

The clinical findings on admission showed a positive sputum with a subsiding temperature and homogeneous density over the entire left chest due to thickened pleura from an old pleural effusion. The trachea was displaced to the left. The right lung showed a compensating emphysema and small lesions in the second and third interspaces. A permanent phrenic nerve paralysis on the left side was advised, to be followed by an upper thoracoplasty for the closure of cavities in the upper left lobe. On April 6, 1938, a phrenic exeresis was carried out without incident. His subsequent course was uneventful for seventeen days. Late in the evening of the seventeenth day he complained of indigestion and abdominal colic. Two enemas were fairly effective without relief of the pain. Emesis occurred and continued with gradual development of abdominal distention during the night. Stupes and all other measures were without effect and early the following morning the abdomen was distended and tympanitic with no cessation of pain or vomiting. Scout x-ray plates disclosed dilated ileum with fluid levels, so that the diagnosis of acute intestinal obstruction seemed

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certain. He was immediately prepared for surgery. It is unfortunate that the roentgenologist did not have an opportunity to examine the films before operation as the distended loops of bowel were so peculiarly grouped together in a more-or-less circumscribed mass that it is possible the correct diagnosis might have been made preoperatively.

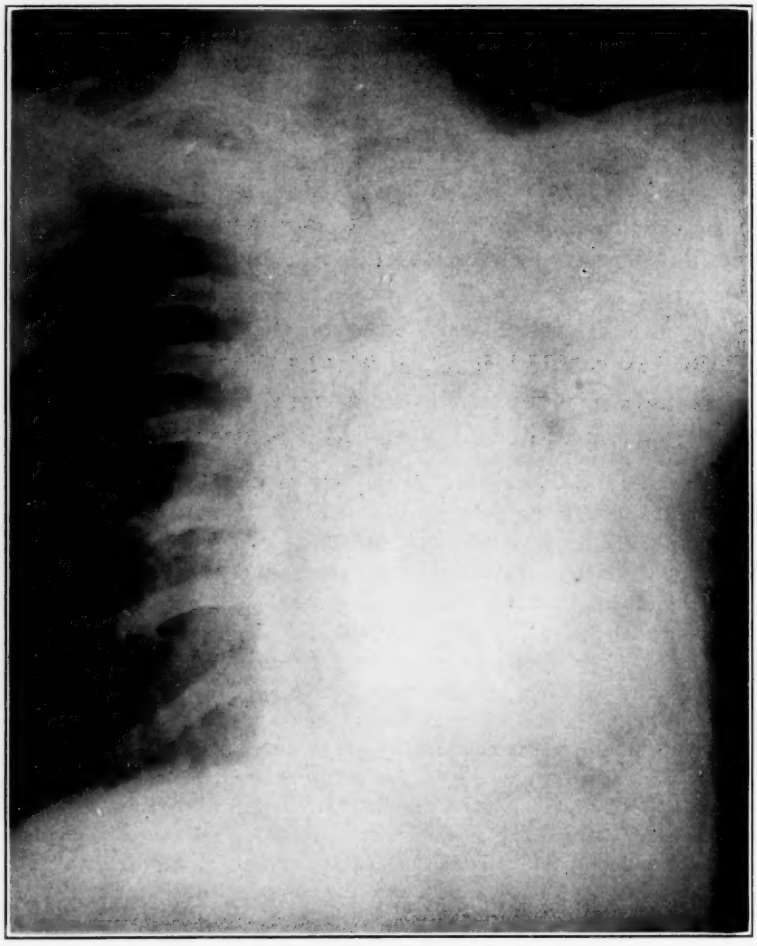

Fig. 1.—Chronic pulmonary tuberculosis with cavitation and thickened pleura on the left.

Under spinal anesthesia combined with cyclopropane inhalations, a right rectus incision was made. On entering the abdominal cavity no intestines could be found in any part of the abdomen. The abdominal cavity was rather tensely filled with a mass resembling an ovarian cyst, which extended well up under the costal margin and down into the pelvis. Intestines could be seen beneath the surface of the mass. It was recognized as a retroperitoneal hernia but after prolonged search no point of entrance into the sac could be made out. The sac, therefore, was opened through an avascular portion and the intestines allowed to extrude from the sac. It was then found that the neck of the sac opened to the left and that the first portion of the jejunum was incorporated in its wall. The intestine was then reduced through the neck of the sac with some difficulty because of distention of the various loops. The

circulation of the bowel did not seem seriously impaired and there were no adhesions in the sac. Further examination showed that the superior mesenteric vessels were in the anterior margin of the sac and that the opening was placed between the first portion of the jejunum and the cecum, lying slightly to the right of the spine. All of the small intestine except a terminal two or three inches of the ileum was enclosed within the sac. The anterior margin of the neck of the sac was then sutured to the posterior abdominal wall close to the first portion of the jejunum, thereby closing the neck of the sac, care being necessary to avoid the superior mesenteric vessels. The opening first made in the wall of the sac was also closed by suture and the abdomen was closed with some difficulty. The patient's condition at the close of the operation

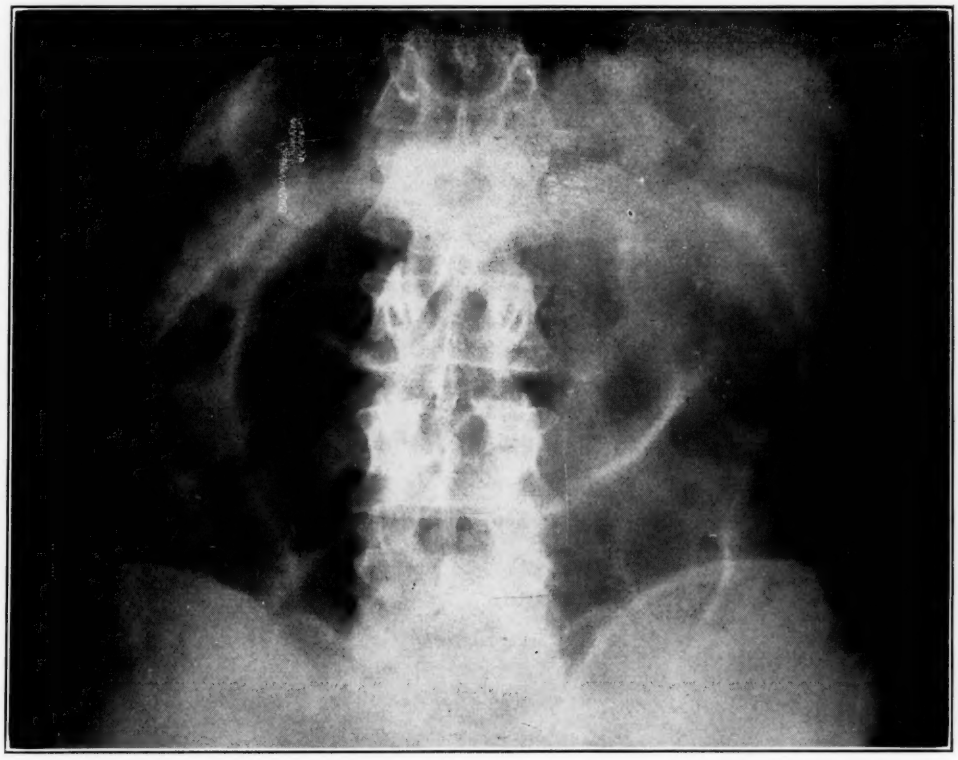

Fig. 2.—Scout film of the abdomen, showing dilated ileum over most of abdomen, but all confined within a circumscribed area.

was fair, showing an increase of pulse rate from 112 to 136. He was given 5 per cent glucose and acacia during the operation, and subsequent transfusions. Wangensteen drainage and an oxygen tent were employed, together with the usual postoperative measures used in intestinal obstruction. The drainage from the tube gradually changed from fecal to a clearer appearance and reasonable hope was held for recovery but two days after operation pneumonic consolidation of the right base of the lung terminated in death of the patient. Unfortunately an autopsy could not be obtained.

In retrospect we regret that our diagnosis was not more accurate and further that acute obstruction was necessary to call the condition to our attention. As previously stated, the history of intermittent partial intestinal obstruction was not obtained at the time of his admission to the hospital.

ETIOLOGY

Neubauer in 1776 discovered "an exceptionally rare case of a peritoneal sac holding all of the small intestines." From this time the literature is rather profuse in the description of various folds and pockets scattered about the abdomen which were thought to be the possible points of origin of retroperitoneal hernias. It remained for Treitz in 1857 to bring order into the general thought by describing various fossae about the duodenojejunal junction which he thought were the probable beginnings of retroperitoneal hernias. He believed that these fossae were expanded and deepened by pressure and the peristaltic movement of the

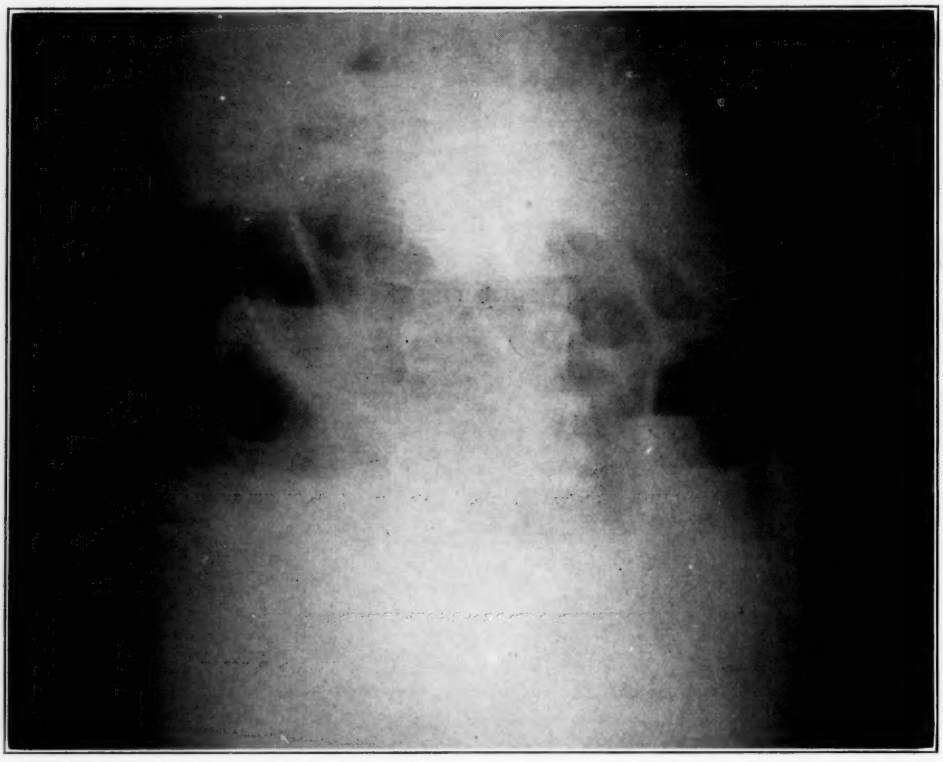

Fig. 3.—Patient in erect position, showing dilated ileum and fluid levels all confined within a circumscribed area.

intestine until a true hernia with a sac was produced. Subsequently authors have generally amplified this conception, the most noteworthy contribution being that of Moynihan on retroperitoneal hernias. He enumerated nine fossae located about the duodenojejunal junction, only five of which he considered of practical importance. He felt that the ultimate size of the hernia depended on the laxity of the retroperitoneal tissue and the extensibility of the peritoneum. Subsequent authors accepted this general idea as to origin without question, ascribing the development to a postnatal period, although Vogt described such a hernia in a newborn infant and Broesike in a child 14 days old.

It remained for Andrews in 1923 to question seriously this mode of origin. He felt that the entire conception was absurd and grotesque. To support his claims he held that:

1. Differential pressure in the abdomen is entirely lacking. All fossae or pouches are enclosed within the abdominal cavity, none extending outside the abdominal wall and therefore pressure at all points must be equal.

2. There are literally hundreds of similar folds and fossae in the peritoneum which rarely if ever are the site of hernias.

3. In all but a few cases the degree of herniation has been total or subtotal.

4. Vogt and Manski report hernia in the very young and the newborn.

5. The hernial sac never contains anything but small bowel. Omentum so commonly found in other hernias is strangely absent.

In brief, his opinion is that hernias are caused by a "congenital anomaly in the development of the peritoneum."

In Andrews' discussion of the embryologic development of the gastrointestinal tract, he postulated that, while the small intestine is developing rapidly from the original single loop, the colon is more retarded. As the colon finally passes across the abdomen from left to right, its mesentery forms the transverse mesocolon. The cecum grows even more slowly not starting its downward migration to the right iliac fossa until the hepatic flexure has been established. In its final position its mesentery becomes attached to and fuses with the posterior abdominal wall. If in the process the small bowel is caught beneath the mesentery of the advancing colon and imprisoned by the fusion of the colon itself to the posterior abdominal wall, all requisites for the formation of a right paraduodenal hernia would be fulfilled. Here the superior mesenteric and the ileocolic artery would lie in the superior margin of the neck of the sac exactly as is found in all right paraduodenal hernias. In a somewhat similar manner he explains the formation of a left paraduodenal hernia, only in this instance the small bowel is caught beneath the mesentery of the descending colon. Longacre has carefully dissected two cases of left paraduodenal hernias dying from other causes. He finds in the course of the blood vessels and in the presence of paraduodenal fossae which were not concerned in the hernia much to confirm Andrews' conclusions.

Brown in 1925 described a case of intraperitoneal right duodenal hernia which, together with a similar case of Sir Astley Cooper in 1807, have been considered as difficult if not impossible to explain as originating in the fossa of Waldeyer according to the explanation of Treitz. It is interesting that recently a third case in a 3-months-old infant has been carefully dissected by Paul and Hill and they find that "the present hernia did not commence in a fossa on the posterior abdominal wall at all, but in one on the side of the mesentery."

Apparently Andrews' ideas are gaining in favor although they are not fully accepted by all authors. Certainly the thought is logical and the presence in the newborn of such hernias is difficult to explain on any but an embryologic basis.

DESCRIPTION

A right paraduodenal hernia, as previously stated, carries the superior mesenteric artery close to the margin of the neck of the sac and the opening of the sac points to the left. The ascending colon may lie to the outer side of the sac, may pass across its surface, or as in the case of Harris the ascending colon may lie along the superior margin of the sac with the cecum in the left hypochondrium. The variations in location apparently depend upon the laxity of the mesocolon or, stating the question in another manner, the degree of fusion with the posterior abdominal wall. While a right paraduodenal hernia commonly occupies the right side of the abdomen, Paul and Hill describe a right paraduodenal hernia which occupied the left side by reason of a rotation of the hernial sac to the left.

A left paraduodenal hernia has the opening of the sac pointing to the right. The anterior margin of the sac carries the inferior mesenteric vein and the ascending branch of the inferior mesenteric artery. Careful dissection by Callander and Longacre has shown that the mesentery of the descending colon beneath these vessels is particularly lax in the developing fetus and as the vessels offer resistance the invagination always occurs beneath these vessels. As a result the opening of the sac is always in this one particular location. The descending colon lies to the outer side of the hernia, although it may be displaced medially. Some hernias contain only a few inches or feet of small intestine rather than the total length of the small bowel. There is no certain reason why only a portion of the bowel could not be invaginated into the mesocolon rather than the entire length. No instance has been reported of colon or omentum being found in such a sac. Pericecal hernias of very rare occurrence could be accounted for in a similar manner.

Broesike emphasized a fusion of the first part of the jejunum with the posterior abdominal wall. In these cases only the efferent loop of the gut may be seen to pass through the hernial orifice, the afferent loop entering retroperitoneally from above. Moynihan makes this the basis for division of right paraduodenal hernias into two types to which he assigned involved nomenclature, depending on whether the first portion of the jejunum was free or retroperitoneal. It would seem that the only logical way to explain this condition is on an embryologic basis. Certainly a retroperitoneal jejunum is difficult to explain as a postnatal development.

Baumeister and Hanchett recently have reported a case of right paraduodenal hernia in which the opening of the sac pointed to the left through which the intestines entered, as should be expected, but the sac

also had a second opening on the right lateral wall outside the colon. They feel that this circumstance is more in line with the theory of Treitz and is difficult to explain by Andrews' conception. In their case they state that the patient received a severe blow on the abdomen from the steering wheel of her car when the car turned over one and one-half times seven years before the onset of her present trouble. It is difficult to avoid the conclusion in their case that the lateral opening of the sac was the result of a rupture from trauma and should not be considered in etiology.

OCCURRENCE

Paraduodenal hernia may be observed at any age. Its occurrence is relatively rare. In 1930 Masson and McIndoe were able to report a total of only 3 cases from the Mayo Clinic up to that time, 1 left and 1 right, both found at autopsy and a third operated upon with recovery. Brown in 1915 reported a total of 32 right-sided cases, in 15 of which operation had been performed, with recovery in 4. The other 17 cases were found at necropsy. Credit for the first successful cure of a right-sided hernia belongs to Newman in 1898 and the second to Carson in 1912.

Byron in 1935 reported 43 cases of right paraduodenal hernia, of which 26 were operated with 14 recoveries and 12 deaths. He also reported 162 cases of left paraduodenal hernia from a survey of the literature.

Left-sided paraduodenal hernias are approximately four times as frequent as right and statistics also indicate that the operation for right paraduodenal hernia is particularly hazardous, being five times more fatal than for the left.

DIAGNOSIS

In 1923 Nagel reported that not a single case of right-sided hernia had been diagnosed before operation and of 91 cases of left duodenal hernia collected by Pikin only 3 were clinically diagnosed. Exner in 1933 states that the credit for the first preoperative diagnosis of a right-sided hernia should go to Taylor who made the diagnosis in one of his cases by x-ray. Exner's report in 1933 was the second diagnosis correctly made.

In certain cases the symptoms have been entirely in abeyance and the condition entirely unsuspected at necropsy. In others symptoms of a vague dyspepsia suggesting gastric or gall-bladder pathology may induce prolonged medical therapy. When the symptoms are more acute, they assume the picture of subacute or acute partial intestinal obstruction. Intestinal colic, particularly after a heavy evening meal, may precipitate an attack. Vomiting is uncommon, except in complete obstruction. The vomitus contains bile. Fecal vomitus is rarely seen because of the high obstruction. Repeated attacks of colic are associated with abdominal soreness and distention relieved with the passage of gas along the intestine. Visible peristalsis and a palpable resonant, gurgling, balloon-like

tumor in the lower abdomen, later involving the entire abdomen, are considered by Moynihan to be the most significant diagnostic signs. The x-rays in our case should have made the diagnosis even without the use of barium as the intestines, although definitely obstructed, remained circumscribed in a definite limited oval area. Exner says that the clumped appearance of the intestinal coils, as if they were contained in a bag, is the most characteristic sign of right paraduodenal hernia.

TREATMENT

The treatment is surgical. Fortunately several cases have been explored for pathology in the absence of obstruction in which situation the hernia can be handled with some ease. In the presence of acute obstruction the situation is quite different. It is essential first to recognize the pathology and secondly, to determine whether a right or left hernia is present. If the sac can be found it may be possible, with gentle dilatation of the neck of the sac, to reduce the hernia. Caution should be maintained not to injure the important vessels lying along the anterior margin of the sac. Adhesions about the neck of the sac are frequently encountered. If, as in our case, the neck of the sac cannot be readily localized the sac may be opened through an avascular portion; the contained intestines extruded and the neck of the sac approached from the inside. Strangulation and necrosis demand resection of the bowel. Adhesions between the loops of the bowel are rare except at the neck of the sac. The neck of the sac should be closed after freeing the bowel to prevent recurrence. Recurrence has been reported in two cases where this has not been done. If reduction is not possible the neck of the sac should be enlarged as much as possible to prevent obstruction. The fortunate case is one with a wide neck and no adhesions to divide, for this permits easy reduction with minimum shock and a good chance for recovery.

SUMMARY

A case of right paraduodenal hernia has been presented which had a long history of intermittent intestinal obstruction and a final severe total obstruction. The long history of advanced pulmonary tuberculosis greatly obscured the picture and the further fact that the patient was never seen in an attack by a physician partly mitigates the oversight. The flat plate of the abdomen should have been of greater diagnostic value, but it was not recognized as indicating more than an acute intestinal obstruction. The thought occurs: Could the phrenic exeresis done seventeen days before the terminal obstruction have been a factor in producing the final picture?

REFERENCES

Abraszow, Von Haberer, Slaudenmeyer: Quoted by Longacre.
Andrews, E.: Duodenal Hernia—A Misnomer, Surg., Gynec. & Obst. 37: 740, 1923.
Averbach, B. F.: Right Paraduodenal Hernia, Am. J. Surg. 35: 128, 1937.

Ball, C. F.: Left Paraduodenal Hernia; Two Cases, One With Rupture Through Wall of Hernia Sac, Am. J. Surg. **29**: 481, 1935.

Baumeister, Carl, and McMicken, Hanchett: Right Paraduodenal Hernia; a Case Favoring the Theory of Treitz, Arch. Surg. **37**: 327, 1938.

Brown, F. R.: Right Duodenal Hernia; Report of a Case Successfully Operated On; Fourth Recorded Recovery, Brit. J. Surg. **13**: 367, 1925.

Bryan, R. C.: Right Paraduodenal Hernia, Am. J. Surg. **28**: 703, 1935.

Callander, C. L., Rusk, G. Y., and Nemir, A.: Mechanism, Symptoms and Treatment of Hernia Into Descending Mesocolon (Left Duodenal Hernia); Plea for Change in Nomenclature, Surg., Gynec. & Obst. **60**: 1052, 1935.

Carson, H. W.: A Case of Right Duodenal Hernia, Proc. Roy. Soc. Med. **5**: 214, 1912.

Cofer, O. S., and Phillips, H. S.: Duodenal Hernia, Ann. Surg. **94**: 1088, 1931.

Coley, B. L.: Strangulated Left Duodenal Hernia; Report of Case With Recovery, Arch. Surg. **18**: 868, 1929.

Coley, W. B., and Hoguet, J. P.: Retro-Coecal Internal Hernia, Ann. Surg. **90**: 765, 1929.

Deaver, J. B., and Burden, V. G.: Right Paraduodenal Hernia, S. Clin. North America **9**: 1013, 1929.

Dowdle, E.: Right Paraduodenal Hernia, Surg., Gynec. & Obst. **54**: 246, 1932.

Emenhiser, L. K., and Panpratz, D. S.: Left Intraperitoneal Hernia; Case, Am. J. Surg. **34**: 104, 1936.

Exner, F. B.: The Roentgen Diagnosis of Right Paraduodenal Hernia, Am. J. Roentgenol. **29**: 585, 1933.

Harris, V. C. J.: Retro-Peritoneal Hernia, Lancet **2**: 240, 1932.

Judd, J. R.: Mesenteric Defects With Special Reference to Their Etiology and Report of Rare Case of Colonic Obstruction, Surg., Gynec. & Obst. **48**: 264, 1929.

Longacre, J. L.: Mesentericoparietal Hernia; Duodenal Hernias of Treitz, Surg., Gynec. & Obst. **59**: 165, 1934.

Lower, W. E., and Higgins, E. C.: Retroperitoneal Hernia, Ann. Surg. **82**: 576, 1925.

Masson, G. C., and McIndoe, A. H.: Right Paraduodenal Hernia and Isolated Hyperplastic Tuberculous Obstruction; Comment and Report of Case Affecting Jejunum and Ileum; Operation and Recovery, Surg., Gynec. & Obst. **50**: 29, 1930.

Mayo, C. H., and Magoun, J. A. H.: Postoperative Intra-Abdominal Hernia, Arch. Surg. **4**: 324, 1922.

Nagel, G. W.: Right Paraduodenal Hernia, J. A. M. A. **81**: 907, 1918.

Neuman, A.: Ein Fall operativ geheilter Hernia retroperitonealis mesentericoparietalis, Deutsche. Ztschr. f. Chir. **47**: 476, 1898.

Novak, E., and Sussman, A. A.: Right Paraduodenal Hernia; Recovery After Operation (the Third in Medical Literature), J. A. M. A. **82**: 1664, 1924.

Paul, M., and Hill, W. C. O.: Right "Duodenal" Hernia, Brit. J. Surg. **25**: 496, 1938.

Porritt, A. E.: Retroperitoneal Hernia; 2 Cases, Lancet **2**: 1156, 1934.

Sammis, J. F.: Mesenteric Hernia in a Babe, Internat. Clin. **3**: 215, 1923.

Short, A. R.: Retroperitoneal Hernia: With Report of the Literature, Brit. J. Surg. **12**: 456, 1925.

Steinke, C. R.: Hernia, Internal; 3 Additional Case Reports, Arch. Surg. **25**: 909, 1932.

Taylor, J.: The X-Ray Diagnosis of Right Paraduodenal Hernia, Brit. J. Surg. **17**: 639, 1930.

Vautrin: Rev. de Chir., Paris **35**: 46, 1907.

INGUINAL HERNIOPLASTY: A NEW MODIFICATION

Report of 107 Cases

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FEW subjects have a more voluminous literature than that of hernia. There are several reasons for this. First, it is known to exist throughout the whole animal kingdom, true hernia having been observed in fish, amphibia, reptiles, birds, and all so-called lower animals. Second, art and literature show the existence of hernia in ancient man. And third, the result of operative intervention is very far from satisfactory, recurrences ranging anywhere from 7 to 50 per cent in different types of hernia. I would hesitate to add to this literature unless I were convinced that the basic concept and operative technique required radical revision.

The cure of inguinal hernia, like that of any other lesion, depends upon the eradication of the cause and the permanency of the repair. The etiologic factors can be classified thus:

1. Anatomic
   - A. Patent processus vaginalis.
   - B. General or local tissue weaknesses; e.g., chronic disease, split aponeurosis, weak transversalis fascia
   - C. Disproportion between the abdominal capacity and contents; e.g., large tumor or ascites
   - D. Long or low attached mesentery
   - E. Large internal ring
2. Mechanical
   Increased intra-abdominal pressure from within or without
3. Physiologic
   Inadequate trap-door action of the internal oblique muscle. This paper will deal mostly with this physiologic inadequacy and method of correction

While the point of exit of the indirect inguinal hernia, the superficial ring, has been overstressed, the site of origin, the deep ring, has been unduly neglected. Unfortunately the internal ring is rather inaccessible, corresponding to a site half an inch medial to the midpoint of a line connecting the symphysis with the anterior superior spine. Even an exceptionally long finger could only reach it with considerable difficulty and trauma. Nevertheless, the main problem in the cause and cure of the indirect inguinal hernia is the determination of the tonus of and protection afforded to this opening in the transversalis fascia.

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Normally, it is completely or partially covered by the arching fibers of the internal oblique muscle. When these fibers contract, they tend to straighten out their arch and lie in parallel apposition to Poupart's ligament, thus acting as a sliding trap door. McGregor has even gone further and demonstrated the existence of a true sphincter, consisting of fibers of the internal oblique, at this point. He found it particularly well developed in the dog. However, I have failed to find any sufficient bundle of muscle fibers which can be dignified by the term of sphincter, either in vivo or after a careful search in the human cadaver; although there are fibers of different amount and caliber passing down along the cord, parallel to Poupart's ligament. Furthermore, considering the oblique direction of the inguinal canal, passing as it does at different levels through the different layers of the abdominal wall, it would seem that a trap-door closure would be more effective than a sphincteric one, which, in addition, would tend to have a deleterious constricting effect upon the vessels of the cord.

Variations in the position of these arching fibers of the internal oblique in relation to the internal ring have been pointed out by anatomists. Cherner has recently published illustrations showing that the further away from the anterior iliac spine the muscle takes its origin, the less chance there is for adequate protection of the space bounded by the anterior superior spine, the pubic spine, and Poupart's ligament. There are three factors which might account for these variations: first, the character of the embryologic development of the abdominal muscle plate, which permits the muscle component to grow cephalically while the fascial portion remains fixed at the inguinal region; second, the widening of the pelvis with the flaring out of the ilia; and third, the assumption of the erect posture. Thus a change occurs in the direction of Poupart's ligament from an almost vertical to an oblique one, while the fanlike expansion of the internal oblique muscle takes place upward and laterally.

The operation herewith reported has as its rationale: first, elimination of the cause of the hernia, if possible; second, narrowing of the lumen of the opening in the transversalis fascia; third, restoration of the internal oblique muscle to a position in which it can act as a buffer at the internal ring. This muscle restoration is accomplished by lengthening its fascial attachment to Poupart's ligament, thus dragging the belly of the muscle more laterally, without interfering with its normal contractile power. More permanency is secured by the use of fascial strips taken directly from the field of operation, as McArthur advocated years ago, without the necessity of invading another field and still without sacrificing any tensile strength.

Attaching the belly of the muscle to Poupart's ligament as is done in the Bassini operation and all modifications is wrong in principle, as this fixation immediately interferes with the functional activity, resulting in

the usual atrophy of disuse. And later, when or if the sutures are partially or completely absorbed and the muscle tends to assume its former position, its contractile power is even weaker than before the operation, thus favoring recurrence. To the argument that the muscle fixation tends to build up the floor of the canal, it can be stated first, that in an indirect inguinal hernia there is no defect of the floor; and second, that nowhere in the human economy is the muscular system used for such a purpose, its function being locomotion, motion, sphincteric control, and stabilization.

IMPORTANT STEPS IN HERNIOPLASTY

1. Incision: About 2 inches longer than the usual incision.
2. Splitting of the aponeurosis of the external oblique, from the external ring to the muscle fusion.
3. Splitting of cremaster fibers to expose the sac medially to the cord.
4. Retraction of the cord.
5. Thorough isolation of the sac by sharp dissection.
6. High ligation of the sac after defining the edge of the transversalis fascia at the internal ring with clamps.
7. Mattress sutures, narrowing the internal ring cephalad to the cord.
8. Excising a strip of fascia from the medial leaf of the external oblique aponeurosis which is used to make two fascial sutures.
9. Exposure of the internal oblique aponeurosis at its junction with the external oblique aponeurosis.
10. Incision of the internal oblique aponeurosis at and parallel to its line of fusion with the external aponeurosis to well above the level of the internal ring.*
11. Reflection of the internal oblique aponeurosis laterally.
12. Suturing the reflected internal oblique aponeurosis to Poupart's ligament with three chromic catgut sutures and the fascial prepared strips.
13. A chromic catgut or fascial suture also placed above the internal ring.
14. The two edges of the external oblique aponeurosis are brought together with chromic catgut sutures.

In most cases the cord is transplanted, although it is not essential in all cases. The external oblique aponeurosis is resutured, usually without any tension, notwithstanding the previous removal of some of its structure. The skin is closed with interrupted silk sutures.

DIRECT INGUINAL HERNIA

The mechanical problem in this type of hernia is quite different from that of the indirect variety. In fact, many surgeons do not consider

*In direct hernias at this stage a free edge is made of the transversalis fascia and this free edge is included with the sutures, through the internal oblique aponeurosis, and sutured with it to Poupart's ligament.

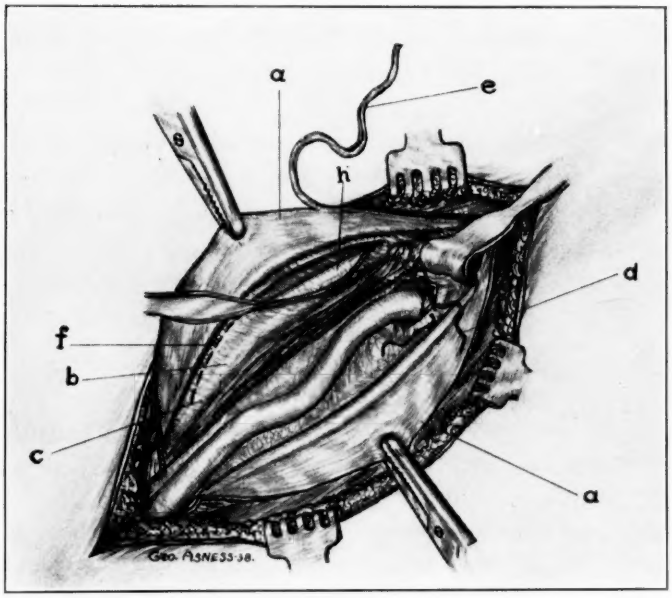

Fig. 1.

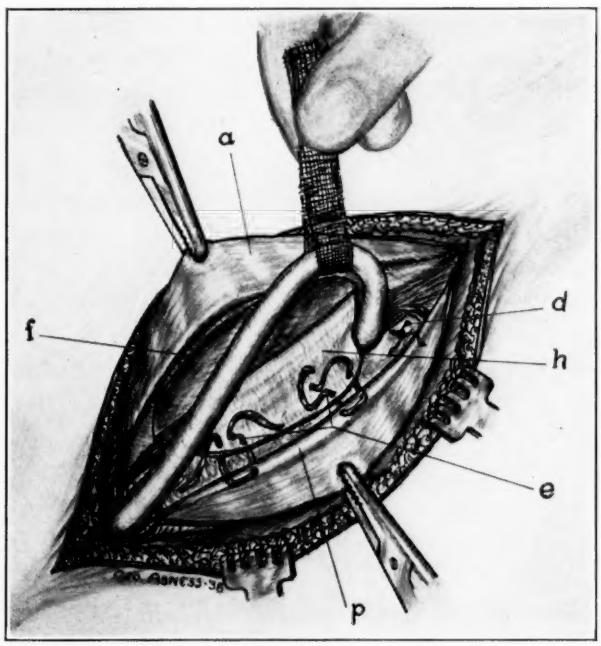

Fig. 2.

Figs. 1 and 2.—*a*, Aponeurosis external oblique muscle; *b*, aponeurosis internal oblique muscle; *c*, internal oblique muscle; *d*, suture through edge of internal ring; *e*, fascial suture taken from external oblique aponeurosis; *f*, incision in aponeurosis internal oblique; *h*, fascial flap from internal oblique aponeurosis; *p*, Poupart's ligament.

it a hernia in the true sense. In the large majority of cases there is simply a relaxation of the distal third (inguinal triangle) of the floor of the inguinal canal. But not infrequently there is a distinct aperture and it is this type that may and does become strangulated. Preoperatively it is impossible to determine which type one is dealing with.

The floor consists normally only of peritoneum and transversalis fascia, the latter covered over and concealed by loose areolar tissue and at the lower angle devoid of any overlying muscular or aponeurotic protection. This fascia, however, is absent at the lateral third of the floor, at which point the fascia dips down into the pelvis.

In the presence of this unprotected area one has a right to expect direct hernias occurring more frequently than the indirect, the reverse of which is the truth. This discrepancy never has been explained satisfactorily. Anatomic variations may be the answer. Whereas normally the internal oblique muscle is inserted into the pubic spine, in a certain number it is inserted into the rectus sheath at variable distances above the spine, thus leaving the inguinal triangle without any muscular protection. Dimensional studies of this triangle have been made both in the cadaver and at operation. Anson and McVay found the median border varied from 0.5 to 9 cm. in length. Polya gives figures up to 7 cm. Andrews' average figure was 5 cm. According to Ssoson-Jaroschewitsch, a greater muscular defect existed in the direct than in the indirect hernias, and the lower fibers of the internal oblique muscle approached nearer a right angle with the rectus sheath.

Based on these and his own observation, Zimmerman in a recent article stated: "From these repeated observations, the conviction grows that the underlying predisposing anatomical basis for direct hernia consists of a congenital absence of adequate muscular support for the lower portion of the inguinal canal. . . . Inasmuch as there are no methods by which muscle can be made to grow where it is deficient, the defect must be repaired by some type of fascial plastic procedure."

With the first part of this statement the writer thoroughly agrees and for the past five years has based his anatomical surgical procedures on this very fact, as stated above. The second part of the statement cannot be accepted as a proper corollary to the first.

Operation.—The object is reinforcement of the floor of the canal, first by closing the aperture in or taking up the slack of the transversalis fascia and second by transplanting the internal oblique muscle nearer Poupart's ligament particularly at its lowest median portion. The approach is the same as for the indirect variety; the cord is retracted well to the side and the floor of the canal exposed from the deep ring to the symphysis. It is most important to clear the transversalis fascia of its overlying areolar tissue, going well underneath the internal oblique muscle. The lateral limitations of the fascia come clearly into view. It

is not sufficient to reduplicate this fascia to Poupart's ligament as many do. A longitudinal incision must be made through it, not including the underlying, nonadherent peritoneum, unless the latter is distinctly sacculated or very large, in which event the excess of peritoneum is excised. The free edge of the transversalis fascia, together with the cut edge of the internal oblique aponeurosis, is then sutured to Poupart's ligament with two or three fascial strips taken from the external oblique aponeurosis and a few chromic sutures. Particular attention is paid to the lowest point of the triangle and all effort made to avoid any tension. The cord overlies the new bed. The external aponeurosis and skin are then sutured.

RECURRENT HERNIAS

It was in this type that we experienced the greatest satisfaction. The principle and technique were essentially the same as in the primary hernias. Fortunately the aponeurosis of the internal oblique was always available as it had not been utilized or interfered with at the original operation. If difficult to expose at the site of operation owing to adhesions, it was traced down from above. In most cases the external oblique was so fibrous or foreshortened by imbrication that it was not available for fascial strips. In that event only, strips were taken from the fascia lata but not used in Gallie weaving fashion approximating muscle to Poupart's ligament but used as mattress sutures approximating the structures indicated above. In the early series silk was used to reinforce the knots of the fascial sutures. As discharging sinuses persisted for six months, in two cases until expulsion of the silk, the latter has been discontinued and catgut substituted.

Two of the cases operated upon for recurrences had been operated upon three times previously, and two of them were of the sliding variety.

STATISTICS

One hundred and twenty-six hernioplasties were performed without any selection of cases, many of which appeared very unfavorable. Thirteen patients had a follow-up period of less than a year. Four cases have been lost track of and 2 have died, leaving 107 cases. There were 62 indirect hernias, including 1 sliding hernia; 26 direct; 6 direct-indirect; 13 secondary (recurrences), including 5 indirect (two sliding), 7 direct, and 1 Spiegel.

TIME ELAPSING SINCE OPERATION					
YEARS	4	3	2	1	
CASES	17	28	29	15	

AGE DECADE					
10-20	21-30	31-40	41-50	51-60	61-70
5	18	28	17	16	5

Total 89 patients

Sex.—86 males, 3 females

Deaths.—1 due to massive gangrene of urinary bladder
1 due to meningitis, three months postoperatively

Recurrences.—Total, 3.75 per cent

A. Indirect, 0

B. Indirect-direct, 0

C. Direct, 3 cases (11 per cent)

1. Age, 31 years; recurrence left side noticed one and one-half years postoperatively, weak internal oblique fascia noted at operation. Recurrence right side (Bassini) one year postoperatively.
2. Age, 61 years; recurrence one side two years postoperatively; heavy work, superintendent of building.
3. Age, 49 years, one side recurrence, two years postoperatively.

D. Secondary, 0.8 per cent, 1 case

1. Age, 51 years; left side, paretic, recurrent sliding, three and one-fourth years postoperatively.

Note.—All recurrences originally bilateral hernias, none infected.

CONCLUSION

A plea is made for a more logical concept of inguinal hernia.

The importance is stressed of the internal ring and internal oblique muscle in indirect hernia; of the cut edge of the transversalis fascia in the direct variety.

Result in indirect hernia to date seems perfect; in secondary recurrences very excellent; in direct hernia, while there is a definite advance, there is still room for improvement.

REFERENCES

Cherner, M.: Indirect Inguinal Hernia in Light of Newer Interpretation of Anatomy, Ann. Surg. **99**: 577, 1934.

Andrews, E., and Bissell, A.: Comparative Studies of Hernia in Man and Animals, J. Urol. **31**: 839, 1934.

Zimmerman, Leo: Inguinal Hernia, Surg., Gynec. & Obst. **66**: 193, 1938.

Anson, B. J., and McVay, C. B.: Inguinal Hernia, Surg., Gynec. & Obst. **66**: 186, 1938.

Polya, E.: Die Ursachen der Recidive nach Radical Operation des Leistenbruches, Arch. f. klin. Chir. **99**: 816, 1912.

Ssoson-Jaroschewitsch, A. J.: Pathogenese und Behandlung der Leistenbrüche, anatomisch-klinisch beleuchtet, Arch f. klin. Chir. **144**: 352, 1927.

THE RESULTS OF TREATMENT IN CANCER OF THE PROSTATE

A Review of 275 Cases

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INTRODUCTION

THE outlook in cancer of the prostate is admittedly grim and has changed little with the development of modern surgery. Caulk has had no cures in 203 cases; Dolan found no ten-year cures in canvassing seventy urologists in 1937. There are several definite reasons for the poor prognosis:

1. The growth usually originates at a distance from the urethral lumen, Moore finding its origin in the posterior lobe in 73.7 per cent at necropsy.

2. Carcinoma of the prostate usually grows slowly, Chwalla having reported two patients who lived 7½ and 8 years, respectively, after cystostomy. This slow growth leads to the very gradual development of obstruction to urination, and to a corresponding hypertrophy of the detrusor which compensates for the obstruction and postpones subjective symptoms until relatively late.

3. Cancer and benign hypertrophy have their onset at about the same age and present the same symptoms; the patient is likely to accept them as the inevitable accompaniment of old age and to defer consulting a physician until they become intolerable.

As a consequence, local extension usually has attached the prostate to the surrounding structures and metastasis has often taken place by the time medical advice is sought. Barringer found only 16 cancers apparently confined within the prostatic capsule in 351 consecutive cases. Bumpus found metastases to bone in 24 per cent and Ferguson in 30 per cent of the patients x-rayed when first seen. Another bar to cure is the tendency of these tumors to invade the perineural sheaths in the pelvis; such invasion was found by Keyes and Ferguson in 52 per cent, and by Graves, Warren, and Harris in 100 per cent at autopsy.

INCIDENCE

To add to the gravity of the problem, the incidence of cancer of the prostate is apparently increasing. It causes 20 per cent of all obstructions at the vesical neck (Young); it is responsible for 0.6 per cent

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of all deaths, and for 4 per cent of those due to cancer in the male (Caulk). Moreover, prostatic cancer has been found at necropsy in 14 per cent of men of all ages by Rich; in 21 per cent of those past 41 years of age by Moore; and in 23 per cent of males past 70 years of age by Muir. Duff found that the death rate from prostatic cancer among the industrial policyholders of the Metropolitan Life Insurance Company increased from 0.8 per hundred thousand in 1917 to 3.7 in 1928.

There are at least two factors in this increase. First, the development of transurethral resection has heightened interest in all disorders of the prostate and lessened the seriousness of prostatic surgery in the patient's mind, so that many more are submitting to operation instead of resigning themselves to suffering; one gets, therefore, a much more accurate idea of the true incidence of prostatism than one could fifteen years ago.

The second important factor is the increase in longevity which has occurred in the last quarter century, since the frequency of prostatic cancer rises with age; Rich found the lesion in 37 per cent of autopsies on patients between 76 and 80 years of age. The Metropolitan Life Insurance Company has observed that the life expectancy from birth of its industrial policyholders had increased from 46.6 years in 1911 to 60.7 years in 1937. The population as a whole has shared in this increase; during the same time, the birth rate has fallen. These two factors have augmented the proportion of the population living in the cancer age, thus causing a great increase in the number of cases of cancer without increasing its proportionate incidence in any age group.

ETIOLOGY

The cause of the disease is not known. None of the numerous theories thus far advanced has been proved. It is often attributed to irritation from prolonged infection; the great frequency of prostatitis makes this a most difficult question. Hryntschak has described multiple foci of regeneration in the prostate which he regards as perhaps postinflammatory and probably precancerous; they are more common in the areas of predilection for cancer. The question of endocrine influences, of course, must be mentioned in this day and age; it remains to be studied.

DIAGNOSIS

Diagnosis is usually easy but is subject to a number of pitfalls, especially in early or small lesions. If stony hardness and fixation have developed, there is little danger of confusion except with tuberculosis and calculi; to confuse these lesions with cancer is usually due to carelessness rather than to ignorance. The small, hard nodule may require biopsy for satisfactory identification unless one feels, as many

do, that treatment even of early cases is of little use; in this event, observation over a period of time usually will clarify the diagnosis. If one agrees with Young that radical operation is of great value in early cases, one must expose and excise the suspicious area for "fast frozen" section and employ radical perineal prostatectomy if cancer is found.

The value of aspiration biopsy is limited by the ability of the pathologist to interpret the scanty material thus collected. While Keyes and Ferguson had satisfactory results in 86 per cent, this performance is probably difficult to duplicate. If positive, it is conclusive; if negative, valueless. The last statement applies with equal force to biopsy by transurethral resection; the frequent presence of benign hypertrophy between the urethral lumen and the cancer often leads to error, especially in small lesions close to the true capsule, since the cancer itself may escape excision. The presence of osteoblastic metastases in bone is diagnostic but of hopeless import; the same is true of the presence of metastatic cancer in removed lymph nodes.

With all of these measures available, the incidence of error ought to be low in the hands of the careful observer, especially if routine sections are made of all material removed at operation in order to detect the occasional cancer which cannot be palpated because it is surrounded by benign hypertrophy.

TREATMENT

As is evident from the discussion of prognosis, treatment usually fails to effect a cure. Factors already discussed usually postpone the discovery of cancer of the prostate until too late for complete removal. Nevertheless, a good deal of palliation can be secured by thoughtful treatment. The methods in general use may be classified as follows:

A. Curative
   1. Radical prostatectomy
   2. Conservative prostatectomy (enucleation of small "concealed" cancer)

B. Palliative
   1. Diversion of the urine
   2. Irradiation
   3. Surgery
   4. Combinations

The chief obstacle to cure is the low incidence of localized cancer. Barringer found only 16 (4½ per cent) in 351 cases, and Colston reported that Young performed but 36 radical operations in 1,040 cases (3.4 per cent). Nonetheless, Young has had excellent results in the operable cases: 50 per cent of five-year cures, and freedom from re-

current obstruction in the remainder; Smith has had substantially the same results. Neither its mortality of 11 per cent nor the fact that many patients are incontinent after radical perineal prostatectomy destroys its value, since it offers the only hope of cure and the sole reasonable guarantee against recurrent obstruction to urination. Although 50 per cent of five-year cures in operable cases becomes 1.7 per cent of all cases when allowance is made for the rate of operability, the operation deserves more frequent employment since it alone offers any real hope of cure. To do so requires, of course, earlier diagnosis.

Radical suprapubic prostatectomy is, for anatomic reasons, more difficult to perform; it does not permit exploration and biopsy of suspicious nodules in the posterior lobe, and Marion claimed but 3 apparent cures in 48 cases. It is, therefore, but little used.

Enucleation of the cancerous prostate, whether suprapubic or perineal, may be regarded as curative only in those rather rare cases in which the tumor is wholly surrounded by benign hypertrophy with which tissue it may be enucleated. The diagnosis is usually missed clinically but made pathologically. The occurrence of this "occult" cancer has been used as an argument against the employment of transurethral resection on the basis that enucleation will cure patients with this type of lesion while resection will obviously fail to do so. This argument is indefensible because of the incidence and rate of cure of this type of cancer. Von Illyes found 27 of them in a group of 354 prostatic cancers (8 per cent). In a series of 91 such cases, Cunningham, Hirsch and Schmidt, von Illyes, and Bugbee had 27 per cent of 2- to 5-year survivals. Thus not more than 27 per cent of 8 per cent of all prostatic cancers (2.1 per cent) may be "cured" by this enucleation. This percentage is further reduced by the fact that survival for 2 to 5 years is by no means synonymous with cure.

The solution, of course, lies in early diagnosis which becomes possible only when routine rectal examinations are made in all elderly men, or in those rare instances in which a small cancer is associated with a benign hypertrophy which surrounds the cancer and produces obstruction; and then only if the cancer is discovered during the operation so that radical excision may be employed.

The results of palliative procedures are not impressive. Catheterization is not even palliative; the bladder usually becomes infected, necessitating more frequent catheterization; suffering is ordinarily intense before death occurs.

Suprapubic cystostomy is more satisfactory if one overlooks the inconvenience of the necessary tube and bottle; the patient is permitted to live in reasonable comfort so far as the bladder is concerned until the tumor occludes the ureters or kills by dissemination. Bumpus found that postoperative life averaged 57 months with 5 per cent of

5-year survivals, but by no stretch of the imagination can the results be called satisfactory; the patients are uncomfortable and none is cured.

Irradiation has long had its advocates; x-ray is simplest in application; it produces a temporary aggravation of symptoms when obstruction is at all severe; it is not ordinarily applicable to complete retention; it produces a temporary but annoying irritation of the skin and rectum when used in adequate doses. Dolan, in questionnaires returned to him by 63 urologists in 1936, found no instance of a 10-year cure from its use, and but five 5-year cures. It is useful chiefly as an adjuvant to radium and in relieving temporarily the pain from metastases to bone and from infiltration of nerve sheaths. Leddy and Gianturco found 3 patients completely and 21 considerably relieved for from 1 to 7 months; 16 were not benefited. Variations in the technique of application make the evaluation of results difficult.

It is at present rather generally agreed that the use of radium, especially when supplemented by x-ray, often causes shrinkage of the gland with alleviation of the symptoms after an initial aggravation, although Bumpus in 1926 found that patients treated with radium were never cured and lived only one-third as long as those treated by cystostomy. The expense and danger of application of radium by the external route has led to the widespread use of interstitial irradiation, with gold seeds of radon replacing the element itself because the former do not have to be removed. Barringer was able to control about 10 per cent of cancers for five or more years by the use of interstitial radon plus high voltage x-ray. While the seeds may be embedded directly into the exposed prostate, they are usually inserted through the intact perineum by means of special trocars. The inaccuracy of this method is more than compensated for by the lack of complications and by the shortened hospital stay. Of the two operative approaches, the perineal is to be preferred because the urethra is not opened. The suprapubic exposure lately advocated by Keyes and Ferguson is likely to be followed by a fistula if any considerable obstruction is present. However, their report that 14 of 41 patients (34 per cent) were living more than 3 years after treatment deserves attention.

The use of transurethral resection for the relief of obstruction in inoperable cases is too recent to permit wholly satisfactory evaluation, but one gets the impression that it is widely employed. It has been condemned as unsurgical to remove a portion of a malignant growth and it has been alleged that healing will not take place, while recurrence will be prompt. Metastasis is said by some to be favored thereby. Nevertheless, obstruction can be relieved in nearly all cases; the patient is neither encumbered nor discommoded by tubes or bottles; failure of the cut surface to heal is of but little moment if the patient can void comfortably; metastases will occur sooner or later

if operation is omitted; and the patient after resection may secure the benefits, if any, of all types of irradiation.

Bugbee operated upon 52 patients by the transurethral route without an operative death; all were relieved of their retention. Nine died of cancer and 3 of heart disease in from 12 to 44 months; 40 were living from 1 to 48 months; 3 had required reoperation, 2 for recurrent obstruction and 1 for hemorrhage.

Caulk was able to relieve obstruction to urination in 77 per cent of 129 cases. Thirty per cent lived 3 years; 18 per cent, 4; and 5 per cent, 7 years.

Jacobs has reported 15 cases so treated; 4 died of cancer in 3 to 20 months; 3 were not relieved; and 7 were free from obstruction to urination after 1 to 33 months.

Thompson and Emmett followed 107 patients treated with the knife punch with 1 operative death (0.9 per cent). Fifty-six were living from 6 to 48 months, and 51 had died, 24 during the first year after operation; 11 had required reoperation for recurrent obstruction after varying intervals. Most of the survivors were in satisfactory condition so far as urination was concerned.

Partial prostatectomy will relieve obstruction by permitting enucleation of a coexisting benign hypertrophy, or excision with knife or diathermy of the obstructing portion of the cancer itself; in other words, it offers the same benefits as does transurethral resection but at a much greater cost in terms of morbidity and mortality.

Swan and Mintz have reported the average hospital stay for suprapubic prostatectomy to be 14 days before and 30 days after operation; in contrast to this, Thompson has been able to omit preoperative preparation in 60 per cent of patients subjected to transurethral resection and puts the postoperative stay in the average case at 5 days.

The risk of transurethral resection is so much lower than that of partial prostatectomy as to demand its use on that basis alone. Colston found the mortality of partial perineal prostatectomy in 320 cases of cancer to be 6.6 per cent, far lower than can be expected with the suprapubic operation, but from three to six times that of transurethral resection (Caulk, Thompson, Davis).

It is thus apparent that transurethral resection is the operation of choice for the relief of retention of urine in those cases of cancer which cannot be removed in their entirety.

REPORTS OF CASES

The diagnosis of carcinoma of the prostate was made at the University Hospital 275 times from April 1, 1930, to Dec. 31, 1936. The first date was selected because it marks the beginning of my experience; the second, to make certain that at least one year had elapsed since the beginning of treatment in the last case. The following plan

determined the type of treatment used during this period; radical perineal prostatectomy was regarded as the preferred treatment, but was little used because, in a charity service, very few patients are seen early enough to permit its application. In those cases exhibiting local extension or metastases, the degree of urinary retention governed the method of treatment. If it was slight or absent, irradiation was employed, starting with the implantation through the intact perineum of radon in gold needles with a 0.3 mm. wall. This was followed by a course of high voltage x-ray therapy given by Dr. Karl W. Stenstrom, who varied the technique from time to time. In all, 200 kv. were used with a filter consisting of 1 mm. each of copper and aluminum and a half value layer of 1.3 mm. of copper. The target skin distance was 70 cm.; the field, 18 by 20 cm.; and the rate, 20 roentgen units per minute per field.

Up to 1934, an anterior and a posterior field were used, giving 4 to 6 treatments in 7 to 11 days, totaling 800 to 900 r. per field. The maximum dose to the prostate was calculated to be 1,200 r.

From 1934 to 1936, right and left lateral fields were also used, and the number of treatments was increased so that four weeks of treatment were required with a total dose of 1,100 r. to each field. The calculated dose to the prostate was 2,200 r.

Since 1936 the technique has been altered to include a perineal and right and left posterior oblique as well as anterior and posterior fields; lateral fields have been used if the diameter of the pelvis exceeded 20 cm. The dose to the prostate has been increased to 2,600 r. (with scattering) in four weeks. Since this last change was inaugurated, the x-ray therapy has preceded the radon.

If retention of urine was severe, cystostomy was often employed before irradiation during 1930 and 1931 and was followed by irradiation; thereafter it was treated by transurethral resection, except in a very few instances in which the resectoscope could not be inserted or in which the general condition contraindicated resection. When the latter was used, it was planned to supplement it by irradiation after an interval of six weeks to allow the postoperative reaction to subside. Some of the patients failed to return for a part or all of the irradiation, and thus afforded small control series for comparison.

Partial prostatectomy was carried out deliberately for cancer in only a few instances; the remaining prostatectomies were done for what was thought to be benign hypertrophy but which proved to be carcinoma on section; since 1932 nearly all of these cases have been treated by the transurethral operation.

In most instances prostatectomy was also followed by irradiation either with radon, with x-ray, or with both.

One hundred and twelve patients were treated by irradiation only; 102, by transurethral resection with or without irradiation; 29, by

partial prostatectomy with or without irradiation; 11, by cystostomy supplemented in 8 by irradiation; radical perineal prostatectomy was employed 3 times and 18 patients were not treated at all.

RESULTS OF IRRADIATION

Fifty-two patients received x-ray therapy only. The average duration of symptoms before treatment was 31.8 months. Forty-four patients were traced; 37 had died after an average of 8.19 months, and 7 were living an average of 24.5 months. Of these, 1 was well at 48 months, 5 had frequent urination but no retention, and 1 had not been benefited. The range of survival after treatment was 17 to 48 months.

Fifteen patients received radon only. The average duration of symptoms before treatment was 24 months. Thirteen were followed. Of these, 10 were dead after an average of 7.5 months, and 3 were living 35.3 months (12 to 66 months). All 3 survivors were free from symptoms.

Forty-five cases received both x-ray and radon. The average duration of symptoms before treatment was 23 months. Forty-two were traced. Of these, 34 died after an average of 14.6 months, and 8 were living 42.2 months (24 to 72 months); 2 were well; 4 had nocturia three to four times; 1 had slight straining; and 1 had not been benefited.

To summarize, 112 patients were treated by irradiation alone. Ninety-nine were followed (88.3 per cent). The average duration of symptoms was 27.2 months before treatment; 81 (81.8 per cent) were dead after an average of 10.6 months, and 18 (18.2 per cent) were living from 12 to 72 (average 34.2) months. The total duration of symptoms from onset to death was 37.8 months; the total duration of life in the survivors from the onset of symptoms to the time of checkup was 61.4 months.

CYSTOSTOMY

Eleven patients were treated by cystostomy. The average duration of symptoms prior to operation was 24.18 months. All were followed and all are dead. The 3 patients who received irradiation after the cystostomy lived an average of 7.78 months; the 8 who had only cystostomy survived 13.54 months. The average survival in both groups was 11.96 months. Thus, the duration of symptoms from onset to death was 36.14 months.

TRANSURETHRAL RESECTION

One hundred and two patients were treated by transurethral resection; the average duration of symptoms prior to operation was 33.1 months; 95 were traced.

Thirty-four of the followed cases had transurethral resection only; 2 died following operation; 22 (64.7 per cent) are dead after 13.5 months; 10 are living an average of 33.09 months. Of these, 6 are symptom free 18 to 65 months; 3 have only nocturia (16 to 73 months); and 1 has pain in the sacral region. Sixty-three of the followed cases received irradiation after resection, 13 with radon, 8 with x-ray, and 42 with both. Of these, 51 (80.9 per cent) are dead after 13.65 months, and 12 (19 per cent) are living an average of 35.09 months; 4 (6 per cent) are well 16 to 32 months; 7 have nocturia without pain or retention; and 1 is bedfast and requires morphine for pain.

The only influence of irradiation in this group seemed to be a very slight increase in longevity, and a definite reduction of the tendency to recurrent obstruction, of which there were 7 in the 34 treated by resection only, and none in the 63 who received supplementary irradiation.

To recapitulate, 97 of 102 cases treated by transurethral resection with and without irradiation were followed. Two (1.9 per cent) died after operation; 73 died after an average of 13.5 months; and 22 are living an average of 34.18 months. The total duration of symptoms was 46.5 months in those dead, and 67.28 months in those still living. Ten (10 per cent) are symptom free 16 to 65 months.

SUPRAPUBIC PROSTATECTOMY

Twenty-nine were treated by prostatectomy, with 3 operative deaths (10.3 per cent). All were traced. The average duration of symptoms before operation was 19 months. In 7 no other therapy was employed. All are dead after 26.6 months. Twenty-two received irradiation. Of these, 17 are dead after 23.8 months, and 5 are living 57.8 months (30 to 112 months); 4 are symptom free (36, 48, 96, and 97 months); and 1, after 112 months, requires morphine and catheterization. The total duration of symptoms from onset to death averaged 42.9 months; in those living it averages 76.9 months.

RADICAL PERINEAL PROSTATECTOMY

Three patients were subjected to radical perineal prostatectomy. One died of recurrence at six months. One is symptom free 91 months (best result in 275 cases); the other is incontinent of urine but otherwise well after 35 months. The cancer was discovered on physical examination for hernia in the patient living almost 8 years; symptoms had been present 4 months in the one who died; and the patient now living 35 months had had symptoms for 6 years before operation, presumably from a coexisting large benign hypertrophy.

UNTREATED CASES

Eighteen patients were not treated, chiefly because the disease was hopelessly extensive without causing retention of urine, but also be-

cause of absence of troublesome symptoms. Symptoms had been present for 23.95 months before the patients were first seen. Sixteen were traced; 15 had died after an average of 3.1 months; 1 was living 44 months with rather pronounced frequency of urination. The average duration of symptoms from onset to death was 27.95 months.

DISCUSSION

To compare the results of the various methods of treatment is difficult, both because of the small size of the various groups and because the indications for treatment were not precisely the same in all. Nevertheless, nearly all of the patients had prostatic carcinoma which had extended outside the gland itself and which had interfered with micturition. This interference was slight in the group treated by irradiation alone and severe in the others.

Four criteria of the effectiveness of treatment will be used in this discussion, namely: the mortality rate of the various groups as compared to the expected rate in the general male population at the average age (69) of the whole group; the survival after treatment; the duration of life after the onset of symptoms as compared to that of a group of untreated cases; and the numbers of symptom-free survivors.

Figs. 1 and 2 show how carcinoma affected the expected mortality. The top line in each represents the expected mortality rate in the general male population (Dublin and Lotka). The bottom line shows the mortality in 18 untreated controls, and the intermediate lines those in the various types of treatment. They were computed by adding together the deaths in each group during each successive year following treatment, converting the resultant figure to the percentage of that particular group, and starting the graph at the age of 69, which was the average age of the whole group. Thus, for the purpose of the graph, all patients who survived treatment were considered as living at the age of 69; and all deaths occurring in the first year after treatment as having occurred between the ages of 69 and 70. All of the lines, except those pertaining to cystostomy, are necessarily incomplete because there are patients still living in all other groups. It is obvious that the development of prostatic carcinoma increases the mortality rate far above that normally expected, and this without regard to the treatment employed; however, treatment retards the mortality rate very definitely when the untreated controls are considered.

On this basis the best results have followed partial suprapubic prostatectomy supplemented by irradiation, since a higher percentage of patients are living for a longer time than after any other form of treatment. However, these graphs ignore an operative mortality of 10 per cent because it is not chargeable to the disease per se; if this were included, the curve would be less favorable.

Allowance should be made for the fact that practically all of the patients receiving prostatectomy had concealed and, hence, early cancer and for the fact that the last operation in this series was done in 1932, so that more time has elapsed since treatment than in any other group. Moreover, the three radical perineal prostatectomies were included in this group because they were too few to permit the construction of a second graph.

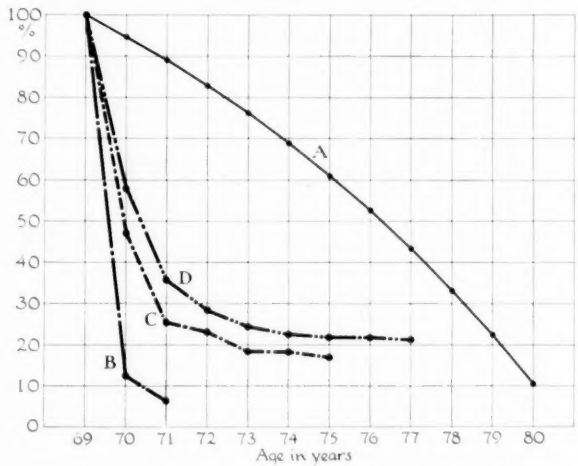

Fig. 1.—Survival after treatment for carcinoma of the prostate. *A*, Expected survival of male population; *B*, survival of untreated cases of carcinoma of the prostate; *C*, after irradiation; *D*, after all forms of treatment combined.

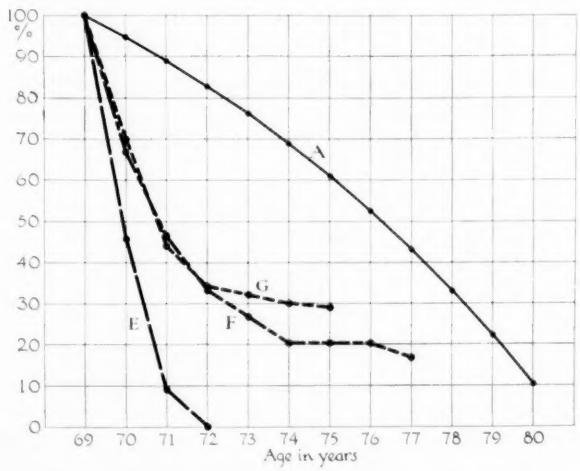

Fig. 2.—Survival after treatment for carcinoma of prostate. *A*, Expected survival of male population; *B*, survival of untreated cases of carcinoma of the prostate; *C*, after irradiation; *D*, after all forms of treatment combined; *E*, survival after cystostomy (with and without irradiation); *F*, after transurethral resection; *G*, after prostatectomy.

When these facts are considered, it is evident that transurethral resection is probably as effective as prostatectomy so far as longevity is concerned, and that it achieves this result at one-fifth the mortality.

When one adds the fact that the hospital stay with transurethral resection is one-third that of prostatectomy, the advantages of the former are still more apparent, except in the case of localized cancer where only radical perineal prostatectomy seems to offer any hope of cure.

There is disappointingly little difference between the results of the various types of treatment when their effect upon the total duration of the disease from the onset of symptoms to death is considered (Table I). As can be seen, this varied from 36.1 months in the case of cystostomy to 46.5 months in the case of transurethral resection (ignoring the single radical perineal prostatectomy). The differences among the various groups are probably not great enough in relation to the total duration of life to warrant consideration. This is also true of the duration of the disease in those still living which varies from a low of 61.4 months with irradiation to a high of 94 months with radical perineal prostatectomy. Even in the untreated group there was one patient surviving more than 5 years after the onset of the disease. In other words, the duration of life after the onset of

TABLE I

RESULTS OF TREATMENT FOR CARCINOMA OF THE PROSTATE

TYPE OF TREATMENT	NUMBER OF PATIENTS	NUMBER TRACED	DURATION (MO.) BEFORE TREATMENT	DURATION AFTER TREATMENT				DURATION OF SYMPTOMS FROM ONSET (MO.)		PATIENTS SYMPTOM FREE		
				DEAD		LIVING		DEAD	LIVING	NUMBER	DURATION (MO.)	%
				NO.	MO.	NO.	MO.					
Irradiation	112	99	27.2	81	10.6	18	34.2	37.8	61.4	6	21.75	7
Resection	102	95	33.1	73	20.7	22	34.1	46.5	67.2	10	29.6	10.5
Partial prostatectomy	29	29	19.0	24	25.2	5	57.8	42.9	76.9	4	69.2	13.9
Cystostomy	11	11	24.1	11	11.9	0	–	36.1	–	0	–	0
Radical perineal prostatectomy	3	3		1	4.0	2	63	8.0	63	2	63.0	66.6
Total	257	237		190		47	38.7	42.06	66.2	22	39.8	9.3
Control series (untreated)	18	16	23.95	15	3.1	1	44	27.05	67.95	0	–	–

symptoms was but little lengthened by any form of treatment. This statement must be qualified by pointing out that both the average survival after treatment and the average survival after onset of symptoms are rendered inaccurate by the fact that many of the patients are still living and may live long enough to bring the averages of the whole group well above the stated figure. Since nearly all of the survivors are old men who still have cancer, this seems improbable.

Best results in terms of length of survival after treatment followed partial suprapubic prostatectomy with 20 per cent of those surviving

operation living an average of almost 5 years after operation. While this is exceeded by radical perineal prostatectomy (66 per cent living 63 months), the latter group is too small to permit the drawing of worth-while conclusions.

When allowance is made for the fact that more time has elapsed since treatment by prostatectomy than by resection, the results from the latter are good enough (20 per cent living 34 months) to suggest that, in the long run, they will equal those of partial prostatectomy.

None of the criteria stated above involves the question of greatest interest to the average patient; namely, the prospect of survival without symptoms. This cannot be determined accurately, of course, since dead patients cannot answer questionnaires and since it is practically impossible to secure adequate information upon this point from the relatives and local physicians of a large group of charity patients. It is, therefore, necessary to fall back upon the number of symptom-free survivors, disregarding the obvious fact that it is more comfortable to live for a year with a normally functioning bladder than to live for two while depending upon a catheter or cystostomy apparatus. On this basis there is little room for satisfaction in any of the groups.

Again, the good showing of radical perineal prostatectomy (66.6 per cent well 63 months) is spoiled by the fact that this is a group of two cases. Partial prostatectomy with irradiation has yielded 13.9 per cent of symptom-free survivors living an average of 69.2 months. This rises to 15.3 per cent if operative deaths are excluded. Transurethral resection stands third with 10 per cent well after 29.6 months, and irradiation fourth with 7 per cent after 21.75 months.

The extraordinarily poor showing of cystostomy is explained by the fact that it was employed only in those patients whose condition was too poor to permit surgical relief of the obstruction to urination, or into whose bladder the resectoscope could not be inserted.

Results in the whole group are not reassuring. Out of 275 patients with carcinoma of the prostate, 257 were treated, and 237 (92 per cent) of these were followed. Forty-seven (15.6 per cent) are living an average of 38.7 months, of which 22 (9.3 per cent of the whole group) are free of symptoms after 39.8 months. Whether any of these has actually been cured is open to question. Most of the data concerning the patients' present status are based upon answers to questionnaires; those who actually returned for examination all had evidence that cancer was present but controlled. The two possible exceptions are those who had radical perineal prostatectomy; neither has any evidence of tumor at present.

It is necessary to mention three desirable results of irradiation which cannot be brought out by these statistics; namely, the relief of pain from extension and metastasis and the distinct diminution of the

tendency to recurrent obstruction after its surgical relief. No data are available to evaluate the former, but it is very definite. The latter is demonstrated by the fact that 7 of the 35 patients treated by transurethral resection alone returned with recurrent obstruction, while none of the 67 who had resection and irradiation did so.

An additional consideration is the clinical impression that the majority of patients receiving only irradiation noticed a distinct improvement in urination.

SUMMARY AND CONCLUSIONS

1. The results of treatment in 275 cases of carcinoma of the prostate are reported. Of these, 253 were followed; 112 were treated by irradiation alone, 102 by transurethral resection supplemented in 67 by irradiation; 29 were treated by partial prostatectomy, 11 by cystostomy, 3 by radical perineal prostatectomy, and 18 were not treated.

2. Of the whole group, 15.6 per cent were living an average of 38.7 months and 9.3 per cent were symptom free an average of 39.8 months.

3. After radical perineal prostatectomy, 2 of 3 patients were well after 35 and 91 months.

4. After partial suprapubic prostatectomy, 4 of 26 (15.0 per cent) surviving operation are well 69.2 months.

5. After transurethral resection, 10.5 per cent of 95 patients are well 29.6 months.

6. After irradiation, 7 per cent are well 21.75 months.

7. No form of treatment has reduced the mortality per year to that for the general male population.

8. No form of treatment has influenced materially the total duration of the disease.

9. Irradiation is of value for the relief of pain, for retarding or preventing the recurrence of obstruction to urination after its surgical relief, and for the relief of low grade obstruction to urination.

10. Transurethral resection accomplishes the same result as partial prostatectomy, with one-fifth the mortality and one-third the hospital stay. It does not cure the disease, but merely relieves the obstruction.

11. Except when localized within the gland itself, cancer of the prostate cannot at present be cured.

REFERENCES

Barringer, B. S.: Prostatic Carcinoma, J. Urol. **33**: 616-20, 1935.

Bugbee, H. G.: Unsuspected Carcinoma of the Prostate Discovered on Section, J. Urol. **22**: 363-76, 1929.

Bugbee, H. G.: Experiences With Transurethral Resection in Carcinoma of the Prostate, Tr. Am. Assn. G. U. Surg. **29**: 207-212, 1936.

Bumpus, H. C.: Clinical Study of 1,000 Cases of Carcinoma of the Prostate, Surg., Gynec. & Obst. **43**: 150-55, 1926.

Caulk, J. R.: Carcinoma of the Prostate, J. Urol. **37**: 832-39, 1937.

Caulk, J. R.: Transurethral Surgery, Surg., Gynec. & Obst. **58**: 341, 1934.

Chwalla, R.: Beitrag zur Therapie des Prostatacarcinoms, Ztschr. f. urol. Chir. **38**: 154-60, 1933.

Colston, J. A. C., and Lewis, L. G.: Carcinoma of the Prostate, a Clinical and Pathological Study, South. M. J. **25**: 696-700, 1932.

Cunningham, J. H.: Treatment of Carcinoma of the Prostate, Boston M. & S. J. **186**: 99-105, 1922.

Davis, T. M.: Transurethral Resection, Urol. & Cutan. Rev. **39**: 372-377, 1935.

Dolan, L. P.: Carcinoma of the Prostate, Urol. Corresp. Club Letter, June 6, 1938.

Dublin, L. J., and Lotka, A. J.: Length of Life, New York, 1936, Roland Press, p. 15.

Duff, J.: Cancer Mortality, Bladder, Kidney, and Prostate, 1917-1928, J. Urol. **32**: 346-353, 1934.

Ferguson, R. S.: Recent Advances in Diagnosis of Carcinoma of the Prostate, Canad. M. A. J. **29**: 497, 1933.

Graves, R. C., Warren, S., and Harris, P. N.: Osseous Metastases of Carcinoma of the Prostate With Special Reference to the Perineural Lymphatics, Tr. Am. Assn. G. U. Surg. **29**: 179-205, 1936.

Hirsch, E. F., and Schmidt, L. E.: Small Carcinoma of the Prostate Gland, J. Urol. **20**: 387-405, 1928.

Hryntschak, T.: Contributo alla patogenesi istologia e statistica del carcinoma della prostata, Urologia **4**: 5-11, 1937.

Jacobs, A.: Transurethral Resection of the Malignant Prostate (With a Review of 15 Cases), Brit. J. Urol. **7**: 321-329, 1935.

Keyes, E. L., and Ferguson, R. S.: Early Diagnosis and Radical Treatment of Carcinoma of the Prostate, Brit. J. Urol. **8**: 346-352, 1936.

Marion, G.: Treatment of Cancer of the Prostate, J. d'Urol. méd. et chir. **21**: 385-96, 1926.

Metropolitan Life Insurance Company: Statistical Bulletin **19**: 2-4, 1938.

Moore, R. A.: Morphology of Small Prostatic Carcinoma, J. Urol. **33**: 224, 1935.

Muir, E. G.: Carcinoma of the Prostate (Hunterian Lecture), Lancet **1**: 667, 1934.

Rich, A. R.: On Frequency of Occurrence of Occult Carcinoma of the Prostate, J. Urol. **33**: 215, 1935.

Smith, G. G.: Total Prostatectomy for Carcinoma, J. Urol. **22**: 377-96, 1929.

Stirling, W. C.: Treatment of Prostatic Cancer, South. M. J. **27**: 590-97, 1934.

Swan, C. S., and Mintz, E. R.: A Review of the Prostatectomies for Benign Hypertrophy at the Massachusetts General Hospital, J. Urol. **26**: 67-90, 1931.

Thompson, G. J.: Transurethral Resection, J. Urol. **3**: 405, 1935.

Thompson, G. J., and Emmett, J. L.: Treatment of Carcinoma of the Prostate by Transurethral Resection, Urol. & Cutan. Rev. **39**: 679-85, 1935.

Von Illyes, G.: Erfahrungsergebnisse bei Nieren-, Blasen-, und Prostatakrebs, Ztschr. f. urol. Chir. **41**: 123-132, 1935.

Young, H. H.: The Radical Cure of Cancer of the Prostate, Surg., Gynec. & Obst. **64**: 472-84, 1937.

THE TREATMENT OF POSTOPERATIVE PULMONARY ATELECTASIS

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IN A MOST complete review of the history of massive pulmonary collapse, Bowen[1] found many instances of its medical recognition during the nineteenth century. Although numerous accurate pathologic descriptions appeared and several instances of its experimental production are recorded, it was not generally accepted as a clinical entity until the Englishman, Pasteur, rediscovered the disease. His first publication on the subject appeared in 1890, to be followed in 1908 and again in 1910[2] by increasingly clear descriptions of atelectasis. This latter paper is generally accredited as establishing the existence of pulmonary collapse, although a much better understanding of the disease resulted from his "Annual Oration on Post-Operative Lung Complications" in 1911.[3]

Gairdner[4] in 1850 first hypothesized that a mucous plug in the bronchus would cause a collapse of the lung. He favored, however, the theory of a ball-valve action occurring at the fork of a dividing bronchus. In 1878 Lietheim[5] actually produced a pulmonary collapse by placing laminaria tents into the bronchi of rabbits. He was the first to show experimentally that collapse occurs as a result of absorption of the trapped gas into the pulmonary circulation. Elliott and Dingley[6] in 1914 reported eleven cases of atelectasis and were firm in their contention that the disease resulted from the plugging of a bronchus with mucus. Further evidence that a bronchial obstruction would cause atelectasis was presented by Jackson and Lee[7] in 1925. They reported a case of pulmonary collapse in a 12-year-old boy with complete relief following bronchoscopic removal of a mucous plug.

Atelectasis was produced experimentally by Lee, Ravdin, Tucker, and Pendergrass.[8] Mucous plugs were removed bronchoscopically from patients and placed into the bronchial trees of dogs. Under deep ether anesthesia these animals promptly coughed up the transplanted mucus. However, after suppression of the cough reflex with large doses of intraperitoneal barbiturates, the mucus was found to remain in situ and there developed a distal pulmonary collapse. Coryllos and Birnbaum[9] produced experimental atelectasis by plugging the bronchus of dogs with toy rubber balloons and expressed the opinion that an obstruction

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of the bronchus is the only etiologic factor of importance in pulmonary collapse. When their balloons were contaminated with pneumococci, infection always developed in the atelectatic lung. Galbraith and Steinberg[10] placed rubber sponges into the bronchi of anesthetized dogs. Within twenty-four hours the air caught in the obstructed lung was absorbed and complete collapse developed. Careful microscopic and gross studies of the involved lung revealed increasing degrees of infection to the point of abscess formation. If, however, the sponge was removed within twenty-four hours, the lung promptly re-expanded, leaving no permanent changes.

That a mucous plug obstructing the bronchus is not the only factor in the production of atelectasis was suggested by Briscoe,[11] who was able to produce varying degrees of collapse in the rabbit by division of the phrenic nerves. Muller, Overholt, and Pendergrass[12] demonstrated the marked reduction in vital capacity following abdominal operations. They expressed the opinion that elevation of the diaphragm and restriction of respiratory movements diminished the air flow through the adjacent lobe of the lung to the point of stasis and favored collapse of the lower lobes. Churchill and McNeil[13] and Powers[14] measured the vital capacity of postoperative patients and demonstrated that a uniform reduction occurred. Webb, Forster, and Gilbert[15] in 1921 published an interesting observation. They placed a normal person continuously in the horizontal position on one side and found that a marked displacement of the mediastinum with opacity of the lung developed on the dependent side. When the subject was allowed to sit up and take a few deep breaths, the mediastinum immediately returned to a normal position and there was complete clearing of the lung. Galbraith and Steinberg[10] introduced a cannula into the right main bronchus of a dog and instituted forced respirations into this right lung only. Windows were then made in both pleural cavities, thus eliminating the negative pressure surrounding the left lung but not obstructing the bronchus. Complete atelectasis with the associated inflammatory changes in the left lung was present within twenty-four hours, during which time the dog was kept alive by forced respirations into his opposite lung. From this experiment they expressed the opinion that obstruction of the bronchus per se is not necessary for the production of atelectasis.

Another possible factor in the production of a bronchial obstruction is the aspiration of saliva during a general anesthetic. Lowenthal[16] performed immediate postoperative bronchoscopies on twenty-one patients reacting from an ether anesthetic. In 76 per cent of these cases saliva was recovered from the trachea and bronchi. The development of an atelectasis following a pulmonary hemorrhage has been described by Heaton.[17] He reviewed seven reported cases and found that in six instances re-expansion occurred spontaneously within two months. The remaining case was relieved by bronchoscopic removal of the clot.

Lander's belief that both obstructive and compression collapse occur gave rise to his classification of atelectasis as either active or passive. However, today there is general agreement that in the final analysis postoperative pulmonary atelectasis is the result of an obstructing mucous plug preventing air from passing into the distal lung and thus allowing absorption of the trapped gas.

It must be recognized that varying degrees of collapse occur: (A) involvement of a whole lung; (B) involvement of one lobe; (C) involvement of multiple patchy areas which usually occur on one side. The viscosity of the obstructing mucus varies with the size of the bronchus occluded. Thin mucus blocks only the small bronchioles and produces a patchy atelectasis; whereas, the thick heavy tenacious mucus is always present in those patients having a massive collapse.

The secondary factors contributing to the development of postoperative pulmonary atelectasis are many.

1. Pre-existing acute or chronic tracheobronchial infections: Acute exacerbations of such disorders are not unusual following a general anesthetic, shock attendant to a major surgical procedure, or simple dehydration.

2. Abdominal operations: By reducing the vital capacity and the respiratory movements, abdominal operations favor the development of atelectasis. Eliason and McLaughlin[18] claim that high abdominal operations are more frequently followed by collapse than operations elsewhere. However, Christopher and Shaffer,[19] from their series of cases, believe that low abdominal operations with trauma to the oblique abdominal wall muscles are more of a predisposing factor than upper abdominal incisions. This is explained by the fact that the internal and external oblique muscles are accessory muscles of respiration.

3. Tight abdominal dressings: Compression bandages over the abdomen tend to elevate the diaphragm, thus diminishing the capacity of the thorax with resulting lung compression.

4. Spinal anesthesia: This is thought by Brown,[20] Brunn,[21] and others to predispose definitely to the development of atelectasis because of an active depression of the respiratory center.

5. Voluntary suppression of the cough reflex: This is a common finding after abdominal operations. It definitely favors the development of a mucous plug by allowing retention of tracheobronchial secretions.

6. Morphine, barbiturates, and other sedatives: These drugs depress the cough reflex and slow respirations, thus favoring retention of mucus in the tracheobronchial tree.

7. Atropine: The dehydrating effect of atropine on the bronchial secretions has often been mentioned as a possible contributing factor. That it may be unimportant is suggested by the fact that atelectasis is just as common following operations under spinal and local anesthesia

when no atropine is given as following a general anesthetic. Beaumont[22] in 1935 advocated the use of atropine for treatment of the shock and collapse accompanying atelectasis.

8. Dehydration: Inspissation of thick or tenaceous tracheobronchial secretions may occur as the result of dehydration from an excessive loss of body fluids in connection with surgical procedures.

9. The position of the patient: The frequency of collapse of the dependent lung following operations necessitating a prolonged unnatural posture has been pointed out by Christopher and Shaffer,[19] Farris,[23] Scott and Joelson,[24] and others. Forced decubitus position definitely decreases the respiratory movement in the dependent chest, prevents adequate elimination of secretions by coughing, and favors incomplete aeration of this lung. Just as the patient with an acute appendicitis seeks a comfortable position and tends to lie on the right side with the knees and body flexed, so does the postoperative patient try to take tension off his wound by assuming a comfortable posture. While elevation in Fowler's position greatly facilitates the act of coughing, it nevertheless keeps both main bronchi dependent and thereby encourages the stagnation of mucus in the bronchial tract.

The established facts regarding postoperative pulmonary atelectasis are as follows: (1) The disease exists in several forms, depending upon the degree of collapse. There may be collapse of multiple small patches, one or two lobes, or the entire lung. Bilateral pulmonary collapse has even been described by Miller and by Sante. (2) The etiology in the final analysis is the presence of a mucous plug which blocks the main bronchus, a lobe bronchus, or a bronchiole. Contributing factors are of secondary etiologic significance. (3) The condition tends to clear spontaneously. (4) Atelectasis tends to recur. (5) Collapse gives rise to an increase in the negative pressure of the involved hemithorax with a shift of the midline structures to the affected side (Elkin[25] and Habliston[26]).

The rational treatment of postoperative pulmonary atelectasis gradually has evolved as the basic pathologic lesion has been clarified. Artificial pneumothorax to overcome the acute respiratory distress caused by mediastinal shift to the involved side has been recommended by Beaumont,[22] Farris,[23] Habliston,[26] Gundry[27] and Lander.[28] In 1938 Zukschwerdt and Lezius[29] reported a series of fourteen cases of postoperative massive collapse. In every case the production of an artificial pneumothorax was followed by the coughing up of viscid mucus with complete clearing of the involved lung within two to five days. In this country it is usually condemned as being an empirical treatment and not attacking the underlying cause. Brunn and Brill[30] have pointed out the inadvisability of causing a pressure readjustment by artificial measures.

Bronchoscopic aspiration of the obstructing mucous plug has been widely acclaimed as it aims at removing the etiologic agent in post-

operative pulmonary collapse. Such observers as Jackson and Lee,[7] Gundry,[27] Brunn and Brill,[30] Coryllos,[31] Hearn and Clerf,[32] Iglauer,[33] and Perrone[34] have stressed the positive relief that may be obtained by bronchoscopy. The obvious disadvantages of this type of treatment are, first, that bronchoscopy may be a very trying procedure when performed on a postoperative patient; second, that competent bronchoscopists are available only in the larger communities; and third, that as the disease tends to recur repeated bronchoscopic manipulations frequently are necessary. This last objection becomes more formidable when one remembers that these patients are newly postoperative, usually having had an abdominal operation.

In May, 1927, Sante[35] made his first report on postural drainage. While fluoroscoping a patient with postoperative pulmonary collapse, he witnessed a complete re-expansion of the lung following a sudden coughing attack which brought up a large plug of mucus. He recognized the important role played by posture in producing this result and advocated, as an effective therapeutic measure for atelectasis, that the patient be rolled back and forth with his involved side up. Some seventy-seven years earlier, in 1850, Gairdner,[4] in discussing bronchial obstructions wrote, "under the influence of an emetic and a forced decubitus on the opposite side to that on which the dulness existed, almost every trace of it had disappeared in thirty-six hours and the dyspnea was entirely relieved." However, to Sante goes the credit of publicizing a type of postural drainage effective in postoperative pulmonary atelectasis. One year later, 1928,[36] in his second article on the subject he advised that bronchoscopic aspiration be instituted when his method of relief had failed.

Scott and Cutler[37] reported in 1928 that postural drainage had in their hands proved ineffectual. Bowen,[1] Brunn and Brill,[30] and Lee, Tucker, and Clerf[38] all point out that postural drainage may be an effective method of treatment, but resort to bronchoscopy without too much delay. Postural drainage has met with a greater success in the hands of Christopher and Shaffer,[19] Sante,[35, 36] and Mathes and Holman.[39]

Hyperventilation of the postoperative patient by means of a mixture of carbon dioxide and oxygen has been widely practiced for a number of years. In 1906 Henderson in discussing acapnia with relation to shock first suggested that inhalations of carbon dioxide might have some beneficial therapeutic use. In 1920[40] he called attention to the use of postoperative inhalations of carbon dioxide and oxygen as a valuable procedure in the prophylaxis of atelectasis and pneumonia. Artificial hyperventilation has now been widely approved as being an important adjunct in both the prophylaxis and treatment of postoperative atelectasis.

On the Surgical Service of the Cincinnati General Hospital about thirty-five cases of postoperative pulmonary atelectasis are recognized every year. The reason for this high incidence is not clearly understood, but it is thought to be largely due to the prevalence of chronic respiratory infections in the patients admitted to this charity hospital. Confronted with this sizable and frequent complication, gradually there has developed a more or less routine method of treatment.

The most reliable prophylactic measures have been found to be hyperventilation with carbon dioxide and oxygen, breathing exercises, hourly changes in position, and adequate hydration. Abdominal binders are regularly used in the support of rectus incisions as they allow the patient to move about more freely in bed and considerably diminish the pain upon coughing. The tendency toward elevation of the diaphragms with attendant lung compression seems to be of secondary importance for, by using a binder, the patient responds more willingly to measures directed toward the elimination of bronchial secretions.

Any patient developing a sudden or unexpected elevation of the temperature or respiratory rate during the first two days after operation is suspected of having atelectasis until proved otherwise. An immediate examination is made by a member of the resident surgical staff. The common positive findings are: shrinking of the involved hemithorax with respiratory lag, a shift of the trachea toward the involved side, and the presence of coarse rhonchi heard on gentle coughing or deep breathing. If a diagnosis is established, the following procedure is carried out.

If not already in use, a tight abdominal binder is applied. The patient is changed from Fowler's position to that illustrated in the accompanying photograph (Fig. 1). The pillow is removed and the head is dropped flat, leaving the knees elevated. A chair is placed under the foot of the bed and the patient turned so that his affected side will be up. The physician then stands behind the patient and places one hand upon the uppermost shoulder rolling the patient slightly forward upon his abdomen. This puts the main bronchus in a true vertical position and secures the greatest gravitational effect on the bronchial secretions. The patient is instructed to place his uppermost hand on his abdomen, over his wound, and this is reinforced by the free hand of the physician.

Occasionally, simply placing the patient in this position initiates violent productive coughing. As a rule, however, it will be necessary to coax the patient to cough. In the majority of cases the plug will be loosened by the first guarded cough and an uncontrollable cough reflex set up with the production of a sizable quantity of mucus. Coughing is encouraged until rhonchi no longer can be felt by the palpating hand. It is not uncommon for such a patient to volunteer the information,

"that's all." If this fails, or if the patient absolutely refuses to cough because of incisional pain, there are several other tricks to be tried. Further efforts are aimed at loosening the plug. If this can be accomplished, a fit of coughing will follow regardless of whether the patient attempts to suppress it or not. With this in mind, he is asked to take a few deep breaths. Failing to produce the plug a sharp blow on the back freqently will accomplish the desired result.

There will be an occasional case in which all of the above maneuvers fail. In this event, with the patient still in the correct position, carbon dioxide inhalations are given to increase the depth of respirations and, as pointed out by Perrone,[34] this will not infrequently loosen the plug.

Fig. 1.—The knees are elevated and the foot of the bed raised on a chair. The abdominal binder, patient's hand, and the hand of the physician all reinforce the abdominal incision. The physician's other hand keeps the patient rolled toward his abdomen. This hand also detects the clearing of rhonchi as the mucus is coughed up.

If rhonchi still persist and breath sounds are not coming through the involved lung, the patient is forced to remain in the described position for as long as one-half hour at a time. During this period a steam inhalation of tincture of benzoin is given using an ordinary paper bag attached to a croup kettle. Two things are accomplished. The steam thins out the mucus, and the gravitational effect is enhanced by being allowed to act over a period of time.

This regime is only infrequently used in its entirety as the obstructing mucous plug ordinarily can be produced by simple forced coughing with the patient in the correct posture. Hyperventilation with carbon

dioxide and the use of the croup tent are reserved for those cases in which the usual methods have failed. There has been a marked uniformity of success in relieving postoperative atelectasis by the above described type of postural drainage. The most common cause of failure has been found to lie not with the method, but with its application. It might be well to point out that one of the most common errors noted in this clinic is the failure to drop the patient out of Fowler's position even though he will be turned with his affected side up. This does not alter the dependency of the large bronchi and as a result the effect of gravity is working in the wrong direction.

As no special equipment is needed, the patient may be treated immediately upon recognition of the collapse regardless of the hour of the day or night and as often as is thought desirable thereafter. The most striking relief has been noted to occur in those cases in which the atelectasis is recognized within an hour or two after onset. The longer a lung or lobe is allowed to remain collapsed, the more difficult will be its relief by postural drainage. Coryllos[9] states that atelectasis is merely the forerunner of pneumonia and that, if virulent organisms are present in the obstructed bronchus, some degree of pneumonitis invariably must follow. However, clinical experience supports the contention that early re-expansion of an atelectatic lobe is followed by the prompt return to normal state. Jennings[41] has shown, in one case, that an associated tubular bronchiectasis occurring as a result of atelectasis will clear completely with the passage of time.

This treatment was taken as a matter of course until during the spring of 1938 the resident on the Ear, Nose and Throat Service became interested in securing more cases for bronchoscopy. He inquired as to why there were no cases of postoperative atelectasis on the Surgical Service and was told that the complication occurred frequently, but was invariably relieved by conservative measures. His inquiry led to a careful study of six consecutive cases occurring between April 22 and June 18. It is not customary to take emergency portable x-ray films on these patients as postural drainage is always employed immediately upon recognition of the complication. It is considered of more importance to relieve the atelectasis promptly than to lose the forty-five minutes or one hour necessary to take and develop a portable film. Arrangements were made with the Department of Roentgenology to secure rush portable films during the daytime only. For this reason only three of these six cases were checked by roentgenograms. The remaining three presented physical signs of such clarity that a positive diagnosis could be made.

REPORT OF CASES

CASE 1.—M. M., No. 93317. This colored male, 31 years of age, was admitted to the Surgical Service of the Cincinnati General Hospital on April 21, 1938. A per-

forated duodenal ulcer was closed shortly after admission, using spinal anesthesia. Forty-four hours after his operation there developed a collapse of the right lower lobe of the lung. Several postural drainages produced a number of mucous plugs with a complete clearing of the abnormal physical signs within forty-eight hours.

Pyrexia and respiratory difficulty again developed three days after the first episode and a recurrence of the collapse was demonstrated by physical signs. Postural drainage was again effective in eliminating the obstructing mucous plug. His convalescence from this time on was both afebrile and uneventful.

CASE 2.—F. K., No. 93749. This 34-year-old white male was admitted to the Surgical Service of the Cincinnati General Hospital for the repair of an inguinal hernia. Although he gave a history of having had pneumonia ten times, the physical

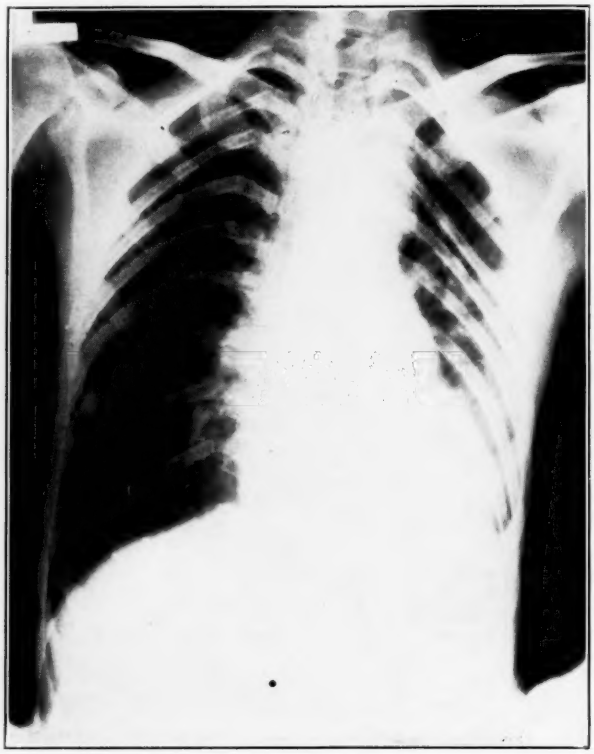

Fig. 2.—There are noted a shifting of the trachea and heart toward the left, narrowing of the interspaces on the left, and a diffuse haziness of the left base (Case 2).

and roentgenologic findings in the chest were normal. A left-sided simple herniaplasty was performed on May 3, 1938, using local field block anesthesia. Twenty-two hours after operation his temperature was 102.4°, pulse 100, and respirations 30 per minute. Telephone instructions were given to leave the patient strictly alone until he could be examined. When seen, he was found to be curled up in bed in low Fowler's position, and lying on his left or operative side. He was coughing feebly and guardedly but was producing no sputum. With every cough rhonchi were clearly audible at some little distance from the bed. He was found to have a diminution of the respiratory movement on the left side with an apparent shrinking of the left chest. There was also a marked deviation of the trachea to the left. A portable x-ray film (Fig. 2) was taken and postural drainage was then instituted. Several

large mucous plugs were obtained and the patient was encouraged to continue coughing until rhonchi no longer could be felt. Fifteen minutes after the first x-ray examination a second film was made (Fig. 3). At this time the collapse was found to have been largely relieved, the respiratory excursions were equal, and the trachea had shifted back to the midline. A second and lesser collapse occurred twenty-four hours later and was promptly relieved by postural drainage. His subsequent course was uneventful and he was discharged from the hospital fifteen days after operation.

CASE 3.—J. M., No. 93966. This white male, 48 years of age, was operated upon for a right inguinal hernia on May 13, 1938. Local field block anesthesia was used. The day following operation he was coughing up thick tenacious mucus, but otherwise was comfortable. Forty-four hours after operation his condition was quite satisfactory, having a temperature of 99.4°, pulse 84, and respirations 18 per minute.

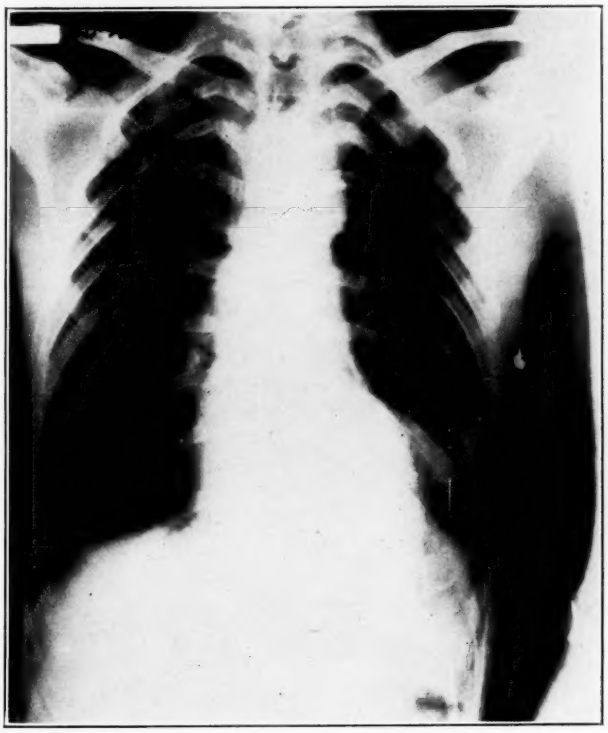

Fig. 3.—This film was taken fifteen minutes later than the film shown in Fig. 2. The trachea is back in the midline and the right border of the heart is now visible. The left base has expanded.

Four hours later his temperature was 102.4° F., pulse 120, and respirations 28 per minute. When examined his trachea was found to be shifted to the right side and the breath sounds did not come through at the right base. Postural drainage produced one large and several small batches of thick yellowish-green tenacious mucus. Following this his trachea was found to be back in the midline, expansion was equal, and normal breath sounds were heard over both bases. Twenty-four hours later his temperature was 99° F. and during his subsequent convalescence did not go above 99.2° F.

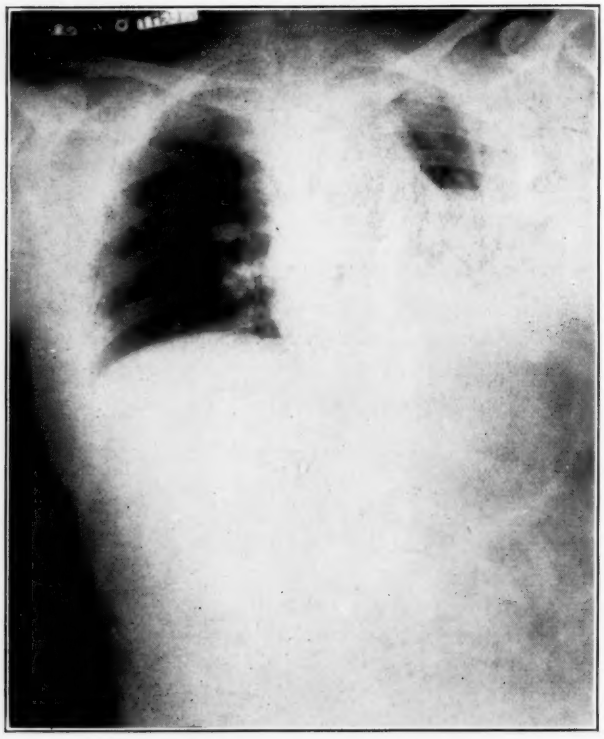

Fig. 4.—The left base is airless and collapsed (Case 4).

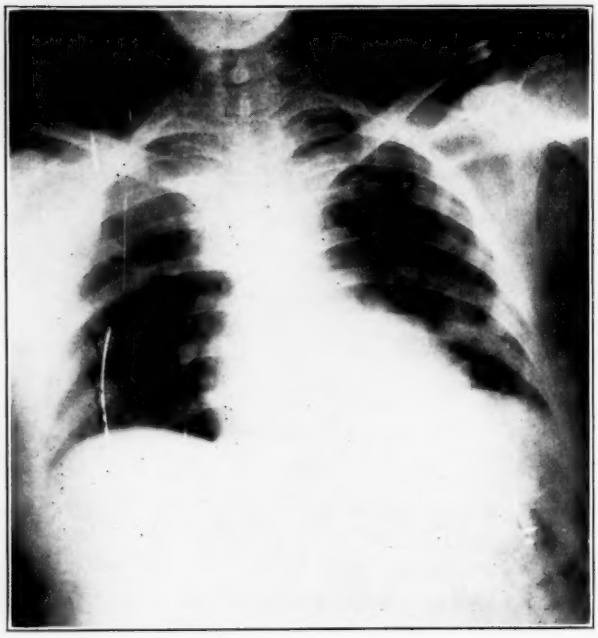

Fig. 5.—This film was taken twelve hours later than the film shown in Fig. 4. There is very little residual haziness in the left base; however, the diaphragm is still slightly elevated.

CASE 4.—O. F., No. 94647. This patient, a white female, aged 27 years, was admitted to the Surgical Service of the Cincinnati General Hospital on May 23, 1938, with a diagnosis of exophthalmic goiter. Following nine days of preparation, a subtotal thyroidectomy was performed under local anesthesia. Thirty-two hours after operation her temperature of 101.8° F. and pulse rate of 120 per minute were not considered unusual. However, within a four-hour period her respirations jumped from 22 to 38 per minute. She was found to have coarse râles scattered through both lungs, but no definite evidence of pulmonary collapse could be discovered on physical examination. The following morning there was discovered an atelectasis of the left lower lobe. A portable x-ray film corroborated the diagnosis and also revealed a shift of the trachea which it had been impossible to detect clinically because of the thyroidectomy (Fig. 4). Postural drainage afforded prompt relief with complete re-expansion as shown by another film taken twelve hours later (Fig. 5). An x-ray film made twenty-four hours later revealed no residual pathologic findings (Fig. 6). The patient was discharged from the hospital eight days after operation.

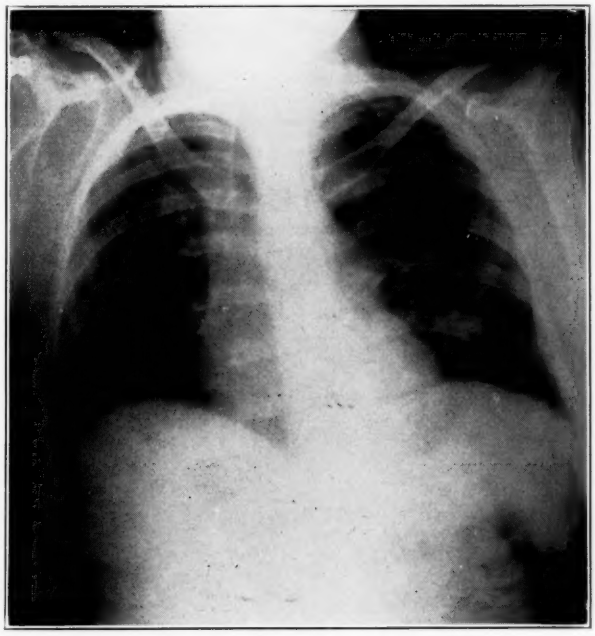

Fig. 6.—After another twenty-four hours, it is noted that complete re-expansion has occurred (Case 4).

CASE 5.—H. E., No. 96506. This 55-year-old white male was operated upon for a left inguinal hernia on June 15, 1938. Local field block anesthesia was used. Twenty-four hours after operation his temperature suddenly rose to 102.6° F., pulse to 116 per minute, and respirations to 30 per minute. Examination revealed a collapse of the left lower lobe as demonstrated by a respiratory lag, a shifted trachea, and alteration of the breath sounds at the left base. As his case occurred during the daytime, an x-ray examination was requested, but it was found that due to technical difficulties there would be some delay. Rather than allow the collapse to remain over this period, postural drainage was instituted and the patient coughed up several plugs of tenacious yellowish mucus. His signs of atelectasis cleared promptly; however, he continued to produce small quantities of sputum during the ensuing

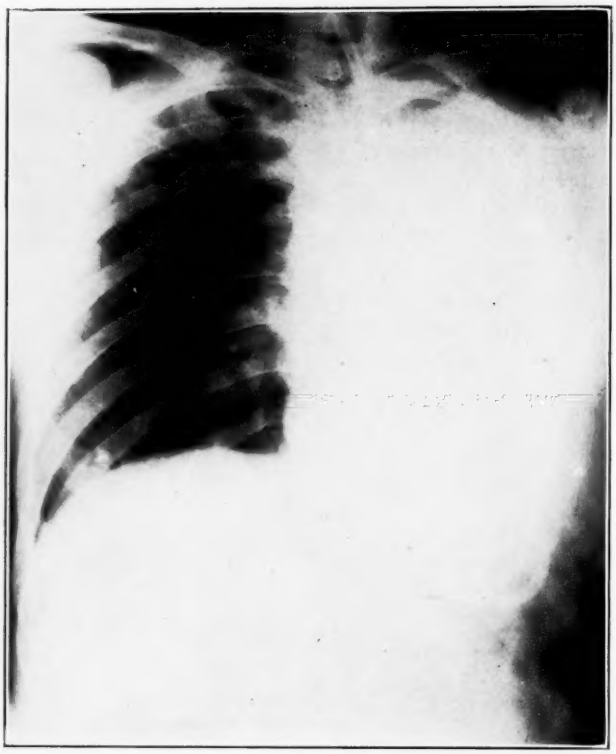

Fig. 7.—This portable film shows complete collapse of the left lung (Case 6). That portion of the duodenal tube that lies in the upper esophagus is seen shifted far to the left side.

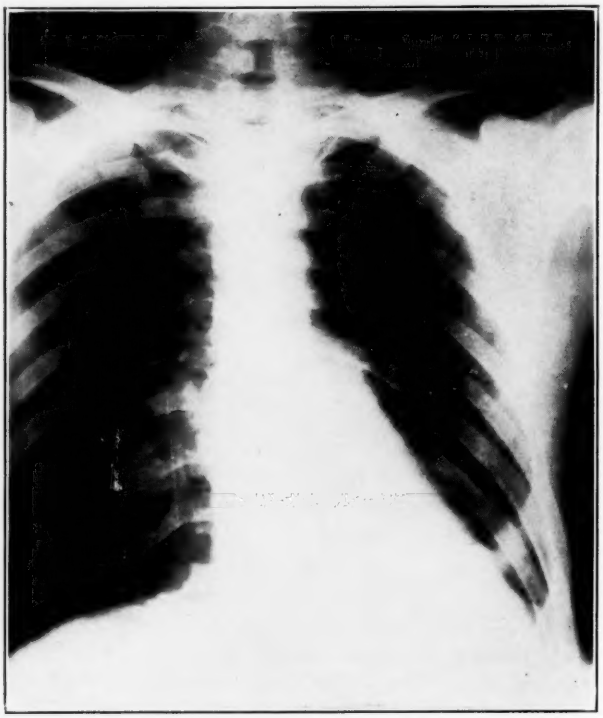

Fig. 8.—Six days after the massive collapse, there is complete aeration of the left lung (Case 6).

week. His temperature spiked at a lower level for the next three days, after which time it remained normal. He was discharged from the hospital on schedule.

CASE 6.—E. R., No. 96648. This patient, a white male, 26 years of age, was admitted to the Surgical Service of the Cincinnati General Hospital on June 17, 1938, because of a ruptured gastric ulcer. Simple closure of the perforation was performed under spinal anesthesia. Twenty-six hours after operation his temperature was 102.4° F., pulse 108, and respirations 40 per minute. As the medical consultant was suspicious of pneumonia, an attempt was made to type the sputum, but no pneumococci were found even after injection into a mouse. A portable x-ray film (Fig. 7) established the diagnosis of massive collapse of the left lung. The indwelling Wangensteen tube nicely demonstrated the shift of the mediastinal structures toward the involved side. Postural drainage produced many plugs of thick tenacious mucus, but it was impossible to clear completely his lungs of rhonchi at any one time. Repeated efforts to bring up the mucus were successful as shown by an x-ray film (Fig. 8) taken six days after the collapse occurred. His convalescence was otherwise uneventful.

COMMENT

Since atropine was not given to any of these patients, it could not have been a factor in the development of atelectasis.

Periodic postoperative hyperventilation with carbon dioxide and oxygen was administered to two of these patients (both ruptured peptic ulcer operated upon under spinal anesthesia). This procedure failed to prevent the development of atelectasis. That this experience has not been unusual at this clinic may be due to the fact that the method used here is not entirely adequate.

As the remaining four patients were operated upon under local anesthesia, no prophylaxis against pulmonary collapse was used. Postural drainage, as described, effectively relieved the collapse in each of these patients in sequence. In two instances there was a recurrence of the atelectasis, but a prompt response was obtained by a repetition of the same therapy.

SUMMARY

Postoperative pulmonary atelectasis results from the occlusion of a bronchus by a mucous plug. Factors contributing to the development of such a plug are: pre-existing tracheobronchial infections, recumbency, dehydration, and suppression of the cough reflex both as a voluntary act following abdominal operations and as a result of sedative drugs. The efficacy of the method of postural drainage used at this clinic for relieving atelectasis is well illustrated by the six cases here presented.

REFERENCES

1. Bowen, D. R.: Acute Massive Collapse (Atelectasis) of the Lung, Am. J. Roentgenol. **21**: 101-141, 1929.
2. Pasteur, W.: Active Lobar Collapse of the Lung After Abdominal Operations, Lancet **2**: 1080-1083, 1910.
3. Pasteur, W.: The Annual Oration on Post-Operative Lung Complications, Lancet **1**: 1329-1334, 1911.

4. Gairdner, W. T.: On the Pathological States of the Lung Connected With Bronchitis and Bronchial Obstruction, Month. J. Med. Sc. **2**: 122-138, 230-246, 1850.

5. Lictheim: Versuch über Lungenatelektase, Arch. Exper. Path. u. Pharmakol. **10**: 54-100, 1878.

6. Elliott, T. R., and Dingley, L. A.: Massive Collapse of the Lung Following Abdominal Operations, Lancet **1**: 1305-1309, 1914.

7. Jackson, C., and Lee, W. E.: Acute Massive Collapse of the Lungs, Ann. Surg. **82**: 364-389, 1925.

8. Lee, W. E., Ravdin, I. S., Tucker, G., and Pendergrass, E. P.: Studies on Experimental Pulmonary Atelectasis, Ann. Surg. **88**: 15-20, 1928.

9. Coryllos, P., and Birnbaum, C. G.: The Syndrome of Pneumococcic Bronchial Obstruction, Arch. Int. Med. **51**: 290-323, 1933.

10. Galbraith, E. G., and Steinberg, B.: The Developmental Mechanism of Pulmonary Atelectasis, Ann. Otol., Rhin., & Laryng. **46**: 800-817, 1937.

11. Briscoe, J. C.: The Mechanism of Post-Operative Massive Collapse in the Lungs, Quart, J. Med. **13**: 293-335, 1920.

12. Muller, G. P., Overholt, R. H., and Pendergrass, E. P.: Post-Operative Pulmonary Hypoventilation, Arch. Surg. **19**: 1322-1345, 1929.

13. Churchill, E. D., and McNeil, D.: The Reduction in Vital Capacity Following Operation, Surg., Gynec. & Obst. **44**: 483-488, 1927.

14. Powers, J. H.: Vital Capacity; Its Significance in Relation to Post-Operative Pulmonary Complications, Arch. Surg. **17**: 304-323, 1928.

15. Webb, G. B., Forster, A. M., and Gilbert, G. B.: Postural Rest for Pulmonary Tuberculosis, J. A. M. A. **76**: 846-849, 1921.

16. Lowenthal, G.: Tracheo-Bronchial Aspiration of Buccopharyngeal Secretion During Ether Anesthesia, Arch. Otolaryng. **21**: 561-573, 1935.

17. Heaton, M. B.: Pulmonary Atelectasis Resulting From Haemoptysis, Canad. M. A. J. **32**: 409-410, 1935.

18. Eliason, E. L., and McLaughlin, C. W.: Post-Operative Pulmonary Atelectasis, S. Clin. North America **14**: 1-12, 1934.

19. Christopher, F., and Shaffer, J. M.: Post-Operative Atelectasis, Am. J. Surg. **32**: 197-203, 1936.

20. Brown, A. L.: Post-Operative Pulmonary Atelectasis, Arch. Surg. **22**: 976-982, 1931.

21. Brunn, H.: Cyclopedia of Medicine, Vol. VIII. Philadelphia, 1933, F. A. Davis Company, pp. 379-388.

22. Beaumont, G. E.: Massive Collapse of the Lung, Brit. M. J. **1**: 314, 1935.

23. Farris, H. A.: Atelectasis of the Lung, Canad. M. A. J. **15**: 808-815, 1925.

24. Scott, W. J. M., and Joelson, J. J.: Post-Operative Massive Atelectasis, Arch. Surg. **15**: 855-870, 1927.

25. Elkin, D. C.: Intra-Pleural Pressure in Post-Operative Atelectasis, Ann. Surg. **86**: 885-889, 1927.

26. Habliston, C. C.: Intra-Pleural Pressures in Massive Collapse of the Lung, Am. J. M. Sc. **176**: 830-837, 1928.

27. Gundry, L. P.: Massive Collapse of the Lungs, Bull. School Med. Univ. Maryland **22**: 77-83, 1937.

28. Lander, F. L.: Massive Collapse of the Lung: "Absorption Collapse," Proc. Roy. Soc. Med. **29**: 1383-1386, 1936.

29. Zukschwerdt, L., and Lezius, A.: The Post-Operative Massive Collapse of the Lung, Chirurg. **10**: 344, 1938.

30. Brunn, H., and Brill, S.: Observations on Post-Operative Pulmonary Atelectasis, Ann. Surg. **92**: 801-835, 1930.

31. Coryllos, P. N.: Post-Operative Pulmonary Complications and Bronchial Obstruction, Surg., Gynec. & Obst. **50**: 795-827, 1930.

32. Hearn, W. P., and Clerf, L. H.: Post-Operative Massive Collapse of the Lung, Ann. Surg. **85**: 54-60, 1927.

33. Iglauer, S.: Post-Operative Atelectasis, Tr. Am. Laryng. Rhin., & Otol. Soc. **42**: 25-34, 1936.

34. Perrone, J. A.: Bronchoscopy as a Treatment of Post-Operative Atelectasis, Pennsylvania M. J. **40**: 842-846, 1937.

35. Sante, L. R.: Massive (Atelectatic) Collapse of the Lung With Especial Reference to Treatment, J. A. M. A. **88:** 1539-1542, 1927.

36. Sante, L.: Massive (Atelectatic) Collapse of the Lung, Ann. Surg. **88:** 161-177, 1928.

37. Scott, W. J. M., and Cutler, E. C.: Post-Operative Massive Atelectasis, J. A. M. A. **90:** 1759-1763, 1928.

38. Lee, W. E., Tucker, G., and Clerf, F.: Post-Operative Pulmonary Atelectasis, Am. J. Surg. **88:** 6-14, 1928.

39. Mathes, M. E., and Holman, E.: Post-Operative Massive Atelectasis, California & West. Med. **31:** 386-390, 1929.

40. Henderson, Y., Haggard, H. W., and Coburn, R. C.: The Therapeutic Use of Carbon Dioxide After Anesthesia and Operation, J. A. M. A. **74:** 783-786, 1920.

41. Jennings, G. H.: Re-Expansion of the Atelectatic Lower Lobe and Disappearance of Bronchiectasis, Brit. M J. **2:** 963-965, 1937.

ARTERIAL INJECTIONS WITH STASIS IN THE THERAPY OF INFECTIONS*

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THE possible usefulness of arteriotherapy was suggested to us by the first arteriogram that we made and immediately afterwards it was applied to certain diseases not only through the arteries of the extremities but also by the aortic and carotid routes. In studying the history of arteriortherapy, it was found that Goyanes,[1] in 1914, first used this method in tuberculous arthritis. Although soon afterwards it was abandoned, nevertheless it is of historical importance. The method was used also by Leriche,[2] in 1913, and by Heddaus,[3] in 1914, and consisted of injecting antitetanic serum by the carotid route. We believe, however, that we are the first to utilize intra-arterial therapy extensively and to apply it by another route; that is, through the abdominal aorta. In 1929 at a conference held in Leriche's clinic in Strasbourg the principles and my observations and results were presented.[4] More extensive investigations were published subsequently by my assistants and myself.[5-10] Whereas Leriche has expressed the opinion that in his experience the value of the procedure has not been found sufficiently convincing, the difficulty of demonstrating the superiority of a method applied to infections diverse in character, localization, and severity, particularly where other methods are also beneficial, is well known. The comparative value of results is of significance only when they are controlled, because it is difficult to deduce the results of therapy based solely upon the clinical impression. Even statistics may not suffice, as in this instance in which the series is too small. One is forced, therefore, to resort to personal experience.

In infections of the extremities arterial injections have been tried in Italy, especially by Luccarelli.[11] In Austria, Demel and Sgalitzer[12] employed abrodil intra-arterially for arthritis. Therapeutic arterial injections have been used most extensively by the French. A review of these observations will reveal that, in general, these investigators consider the procedure valuable.[13-20]

The carotid route has been used by a number of investigators. In 1929 E. Moniz[21] observed the therapeutic effect of sodium iodide injected into the carotid artery in cranial hypertension. Leriche,[2] Heddaus,[3] Fritzsche,[22] and Fourmestraux[23] injected antitetanic serum by the carotid route. Fritzsche employed this method in fifteen severe cases with only

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two deaths. His observation in a case of generalized tetanus, in which at first an injection in the left carotid only had been made, is particularly demonstrative. Whereas the convulsions were bilateral, following the injection they almost disappeared on the right side but scarcely diminished on the left. This demonstrates the significance of the therapeutic action on the cerebral hemisphere corresponding to the carotid injected. The opposite side had received antitoxin only by way of the general circulation.

One of my students, Silveira Ramos, of Angola, has cured a very severe case of malignant malaria by bilateral carotid injections of quinine bromide.[24] Up to 1933, together with other colonial physicians, he has treated 100 similar cases with complete recovery.

In posttraumatic meningoencephalitis we have utilized successfully the carotid route since February, 1929.[4] After publishing our first case, it was later learned that this procedure had been used in America. The experimental investigations of Kolmer, Rule, and Madden[25, 26] using acriflavine, a colloidal solution of iodine, gentian violet, and metaphen, were followed by their clinical application.[27] The first cases of pneumococcic, staphylococcic, meningococcic, and streptococcic meningitis successfully treated in this manner were reported by McMahon,[28] Crawford,[29] Kolmer,[27] and Ersner and Mendell[30] respectively. Finally I desire to call attention to personally observed cases of osteomyelitis of the maxilla and severe infections of the face successfully treated by external carotid artery injections of antiseptics.

The aortic route, however, remains the least employed except by us, apparently because puncture of the aorta is feared, which in our experience is not justified. Thus, all abdominopelvic infections (puerperal or postabortal), peritonitis (appendiceal, perforative, or adnexal), and all ruptures or visceral wounds have been benefited in our experience by this most concentrated, direct, and least toxic method of injecting antiseptics. In my service and in some of the emergency services this is routine. The cases operated upon receive the injections at the end of the operation. The dorsal route is always used because it is simpler and less dangerous than puncture through the open abdomen. The dorsal route of aortic injection may be employed also in blood transfusion, either because venipuncture is difficult or to avoid shock by the venous route.

However, in this presentation I wish to emphasize particularly the most recent modification in technique, especially as applied to the extremities; namely, *intra-arterial injection with stasis.* The principles, as previously stated in 1929 at the conference in Strasbourg,[4] were: "An elastic compression suddenly applied and slowly released can retard the passage of medicaments into the general circulation and can hold them in the tissues. Radiographic proof of this fixation has been obtained in studying a series of arteriograms of the forearm with elastic

compression. Bier similarly observed this phenomenon by using intravenous anesthesia. At first the arterial shadow is visible for about fifteen minutes, then as the vessel loses its opacity the tissues gradually become more accentuated, obviously due to the fixation of sodium iodide in the tissues.''

In spite of these well-established principles, because of its simplicity, for a long time we have performed almost exclusively the arterial injections into the free circulation. However, during the past year, one of my assistants, John dos Santos, studied the problem more intensively. By retaining an active solution in the tissue for a few moments, it is possible to increase its activity and thus reduce the dosage. This has been demonstrated by arterial analgesia. We have observed that novocain injected into the femoral artery in the free circulation produces no regional anesthesia and may produce either a toxic effect or even a rapid general anesthesia. On the other hand, a similar injection with stasis produces an anesthesia of the extremity which is not followed by any toxic manifestations. The tourniquet is removed slowly a few minutes afterwards. The anesthetic agent becomes fixed in the tissues and consequently enters the general circulation very slowly just as in local analgesia. This observation, as well as our serial arteriograms with stasis, explains the action of an antiseptic injected intra-arterially. Thus, with stasis the regional activity of the material injected is increased several times, the dosage can be diminished, and the general toxicity avoided. These facts, which form the basis of the venous analgesia of Bier and the arterial analgesia of Goyanes, contain therapeutic possibilities which have not been utilized.

In arteriography, despite the practice of Kroetz, we prefer the free circulation to obtain the anatomic and functional characteristics of the circulation, but in arterial therapy the problem is different. It is not a question of determining the functional activity which has a diagnostic significance, but of obtaining an action as concentrated, as profound, and as prolonged as possible, without injury either to the tissues or to the vessels.

The following technique has been described by my assistant, John dos Santos: A short, fine needle (0.8 mm. in caliber and 3 cm. in length) with a short point is connected to a rubber tube which in turn is attached to a syringe. Injection through a diseased area should be avoided. The compression is made over healthy tissue above the lesion. In lesions of the proximal or midportion of an extremity it is preferable to use two tourniquets. The distal tourniquet is tightened before the injection; the other, the sphygmomanometric cuff placed proximal to the lesion, is inflated only after the end of the injection. The brachial or femoral artery is then punctured. The application of the tourniquet above or below the puncture is of little or no importance. Facility determines the site of the puncture.

In infections of the hand and forearm puncture of the brachial is performed at the elbow and the tourniquet is applied to the forearm or arm, according to the site of the lesion; but in infections above the elbow it is necessary to inject brachial or the exposed axillary. The avoidance of this difficulty will be discussed later. In the lower extremity the puncture is simple as all regions are accessible for injection without exposing the artery and the tourniquets limiting the diseased zone retain the solution in the desired area.

In performing the injection, it is desirable to have two assistants. In the author's service usually two nurses perform this function. One assistant pumps air into the sphygmomanometer at the desired moment. The other assistant holds the syringe ready to inject the solution. The syringe and the rubber tube are filled with the antiseptic solution. Mercurochrome and 1 per cent acriflavine are the agents most commonly used. The distal tourniquet is tightened until the peripheral pulse has disappeared. The proximal tourniquet, i.e., the sphygmomanometric cuff, is applied to the extremity over healthy tissue and above the lesion. The artery is then punctured and a small red, pulsating stream of blood coming from the needle indicates accuracy of arterial puncture. The rubber tube is then attached to the needle. The assistant injects the solution in the syringe; as soon as this is finished the other assistant pumps up the sphygnomanometer to 300 mm. of mercury. Before removing the needle from the artery, the rubber tube is disconnected from the needle to see if blood still spurts, thus assuring accuracy of injection. Circulatory stasis is maintained for ten to fifteen minutes.

Comment.—The injection at first is not painful, but approximately two minutes after stasis has been produced pain may be experienced and apparently is commensurable to the concentration or quantity of solution fixed in the tissues. Whereas in most cases it can be tolerated, it is desirable, if it is very intense, to administer a general anesthetic. As soon as the tourniquet is removed, the pain disappears. The use of an isotonic solution, as Huet[19] has suggested, should be considered.

Disappearance of pain and decrease in inflammation are the first signs of improvement. The skin reaction is quite distinctive and is characterized by a vasomotor response and a discoloration. In peripheral arterial disease it is very interesting to observe the permeable area of the skin, which becomes red or blue upon injecting mercurochrome or methylene blue, respectively, according to the degree of circulatory involvement. This is a direct Moszkowicz test and therefore has a diagnostic application. Vasomotor phenomena, such as attacks of arterial or venous spasm, occur more frequently in the upper extremity, but this is readily relieved by novacain block of the stellate ganglion. Such attacks have always been stopped by this method and arterial thrombosis has never occurred. The absence of a general reaction is proof that arterial injections with stasis are without danger, particularly because it is possible

to diminish the dosage. John dos Santos has observed that the general feeling of warmth produced by intravenous injection of calcium gluconate remains localized if this method of stasis is used, and, even when the tourniquet is removed, it does not appear. The febrile reactions which occur regularly following intravascular injections without stasis do not develop if stasis is produced. Since this technique has been used, it is our firm conviction that the results are certainly better and superior to the previously employed arterial injections without stasis. The procedure has been applied particularly to the following conditions: (1) Infections of the soft parts, phlegmon, deep abscesses, and especially infections of the hand and foot; (2) acute and subacute osteomyelitis; (3) compound fractures either prophylactically or therapeutically in combating infection; (4) articular infections.

Twenty cases have been treated by this method and its superiority is shown by the rapidity with which the infectious process has been controlled. In some cases this has occurred within twenty-four hours. Disappearance of pain, limitation of diffuse processes, lowering of temperature, and diminution of leucocytosis further characterize its remarkable action. In the majority of cases drainage becomes unnecessary which is particularly important in the forearm, the hand, or the foot. Of considerable comparative value is a case of osteomyelitis of both tibiae, in which we applied arterial injection with stasis only to the worse side. Whereas the infection was promptly controlled on this side, the opposite side drained for a long time.

Only three observations of John dos Santos will be reviewed briefly:

Case 1.—Male, 50 years of age, admitted as an emergency with a phlegmon of the forearm and immediately treated by arteriotherapy with stasis. Tourniquet was applied to the midportion of the arm, and 10 c.c. of 1 per cent mercurochrome were injected into the brachial artery at the elbow. Stasis was maintained for ten minutes. As the phlegmon involved the entire forearm, six small incisions, 2 cm. in length, were made in the upper portion. There was no drainage. Two days later the patient was fever free and practically no suppuration occurred, but as a precaution another injection with stasis was made. The next day there was no evidence of suppuration and eight days later the wound had healed with the exception of superficial cicatrization.

Case 2.—Male, 22 years of age, who fifteen days previously had injured the midportion of the right hand with a bone. Upon admission a very severe infection of the entire right hand was observed. The general condition was very bad, with marked weakness and some delirium. The entire hand and forearm appeared edematous, indurated, and very tender. The fingers were in semiflexion. There was no sign of fluctuation and the leucocyte count was 15,000. Intra-arterial injection of mercurochrome with stasis was done. The next morning practically all the pain had disappeared, the temperature dropped to 37.5° C. and the leucocytosis had decreased to 11,000. That evening the temperature went up to 38° C. and another injection was performed. The next day there was no more pain and the temperature was 37° C. That evening it was only 37.5° C. Finally, on the third day he was fever-free both morning and evening. However, superficial fluctuation was beginning to appear in the forearm and in order to prevent extension of the infection a third

injection was made with stasis. The next day the leucocyte count was 8,800 and a very small localized purulent collection (staphylococcic and a few streptococcic organisms were found) was drained. Following this the wound healed very rapidly. Thus, it may be stated that a very diffuse infection was transformed into an almost aseptic localized suppurative process without fever and without pain.

CASE 3.—Female, 36 years of age, admitted with a phlegmon of the entire forearm which followed an infection of a small wound over the elbow. There was marked edema of the hand and the temperature was 39° C. An intra-arterial injection was made and six minutes of stasis maintained. The pain diminished shortly afterward and the patient was able to sleep. The next day there was limitation of the suppurative process and it was incised and drained. The following day the pain, fever, and edema had disappeared. Six days later the wound had practically healed. This case was less severe than the preceding one as one injection sufficed. However, in the more severe cases it is possible to give the injections once every twenty-four hours and even twice in the same day.

In considering the treatment of infections by a regional, prolonged action of an antiseptic solution in the tissues, it should be realized that this can be accomplished by the venous as well as by the arterial routes. It is possible to obtain regional anesthesia by two methods, that of Bier and that of Goyanes, as has been stated previously. Just as these two surgeons attempted to obtain an anesthetic effect by novocain fixation in the tissues after producing circulatory stasis, we have tried to obtain a therapeutic effect by fixing an antiseptic solution in the tissues also by stasis. Therefore, the stasis is an essential factor. However, it is necessary to consider which is the more preferable route, the arterial or the venous.

At present our experience with the arterial route is more extensive. We have made comparative studies of the two routes which we will present later, but from the physiologic standpoint it seems to us that, in general, the arterial route is preferable: first, because it assures a better distribution of the antiseptic solution in the tissues; and second, because by the use of a tourniquet it permits the solution to be retained in the desired region. Moreover, since it is merely a question of simple puncture, the injection can be performed easily and as often as is necessary. Since in the lower extremity the injection is always made in the groin, the dosage must be slightly increased for infections of the foot and lower leg because of the dilution when it arrives in this distal region. In this area the venous route is probably easier to apply. The injection is made into the internal saphenous below the tourniquet on the leg in the opposite direction of the circulation. In this way the entire foot can be reached, but the solution must be considerably diluted (1 part to 1,000), and the quantity sufficiently great (50 to 100 c.c.). For the thigh, the intravenous method is less favorable (as is the intravenous anesthesia of Bier), because a large dosage of the solution is necessary to fill the venous system up to the capillaries. Thus, the arterial route is preferable for the thigh and the knee; the venous route, easier for the

foot. In the upper extremity the arterial route is certainly better for infections of the forearm and the hand, the puncture being made at the elbow. The venous route perhaps would be better indicated for the arm as the exposure of an artery, which is necessary, would be more difficult than that of a vein.

Finally, if the tourniquet cannot be placed above the lesion, is it still possible to produce the effect of stasis? Yes, this can be accomplished to a less complete degree by compression of the artery after the injection. Thus, the subclavian or the carotid arteries are exposed through a small incision and compression is applied immediately after the injection. Even in aortic injections as a complement to laparotomy (appendicitis, peritonitis following gastrointestinal perforation) it is possible before closing the abdomen to make an injection in the aorta by the dorsal route, which is always easier, and to compress the aorta against the vertebral column for a few moments while the abdomen is still opened.

These directions and principles of the technique are based upon an experience which, up to the present, includes more than 300 cases. Whereas the former type of arterial injection has already made great progress in the treatment of infections, the present method with stasis is considered vastly superior and has the advantage of permitting the use of a less concentrated and a decreased amount of solution.

REFERENCES

1. Goyanes, J.: Tratamiento quimioterápico directo, par la via arterial, de las tuberculosis locales, Rev. clín. de Madrid **12**: 261, 1914.
2. Leriche, R.: Personal communication.
3. Heddaus, A.: Beitrage zur Heilserumbehandlung des Tetanus, München. med. Wchnschr. **61**: 2186, 1914.
4. Dos Santos, R.: L'Artériographie de l'Abdomen et des Membres et Les Horizons de la voie artérielle (Conférence à l'Université de Strasbourg), Med. Contem. **47**: 141, 1929.
5. Dos Santos, R.: La radiografia de las árterias y la terapéutica intraarterial; la viá aórtica, Ars méd. **5**: 189, 1929; Bull. et mém. Soc. nat. de chir. **55**: 589, 1929.
6. Lamas, A.: Thérapeutique par voie artérielle (Communication au 42nd Congrès de l'Association Française de Chirurgie), Med. contem. **51**: 11, 1933.
7. Dos Santos, R.: Les injections intra-artérielles dans les infections hématogènes du rein (Discussion au Congrès de Vienne, Sept., 1936) Lisboa méd. **12**: 1936.
8. Dos Santos, R.: A via carotidiana no tratamento das meningites, Med. contemp. **55**: 1937.
9. Dos Santos, R.: As injeçoes Intra-Arteriais nas infeçoes graves dos membros., Med. contemp. **55**: 1937.
10. Dos Santos, R.: Les injections artérielles avec stase dans la thérapeutique des infections, Mém. Acad. de chir. **63**: 1398, 1937.
11. Luccarelli, V.: Le iniezioni endoarteriose nelle infezione degli arte, Policlinico (sez prat.) **42**: 2255, 1935.
12. Demel, R., and Sgalitzer, M.: Die therapeutischen ergebnisse der arteriographie an den extremitäten, Wien. klin. Wchnschr. **46**: 1017, 1043, 1933.
13. Goinard, Pierre, Mondzain-Lemaire, and Pietri: Injections antiseptique intra-artérielles, Presse méd. **43**: 83, 1935.
14. Arnulf and Frieh, P.: Injections intra-artérielles d'antiseptiques dans les infections des membres, Presse méd. **44**: 629, 1936.
15. Tixier and Arnulf: Mercurochrome intra-artériel dans quelques cas d'infections graves du membre inferior, Lyon chir. **32**: 715, 1935.

16. Santy, P., and Frieh, P.: Des indications de la thérapeutique intraarterielle par les colorants à propos de quelques faits clinique, Lyon chir. **33**: 461, 1936.
17. Huet, P., and Bargeton, D.: Sur quelques effets des injection intraartérielle, Presse méd. **44**: 677, 1936.
18. Ricard, M., and Huet, P.: A propos des injections intra-artérielles antiseptique dans les infections grave des membres, Mém. Acad. de chir. **63**: 35, 1937.
19. Huet, P.: Sur les effets des injections intra-artérielles, Prat. méd. franç. **17**: 436, 1936.
20. Fredit: Presented before the French Surgical Congress, October, 1937.
21. Moniz, Egas: Trois nouveaux cas de cure, au moins provisoire, du syndrome d'hypertension cramenne par les injections intracaratidiennes d'iodine de sodium, Rev. neurol. **1**: 1135, 1929.
22. Fritzsche, E.: Beitrag zur intraarterillen serumbehandlung des tetanus, Chirurg. **8**: 450, 1936.
23. De Fourmestraux, J.: La voie arterielle dans le traitement du tétanos, 3 observations, Mém. Acad. de chir. **63**: 550, 1937.
24. Ramos, Silveira: Personal communication.
25. Kolmer, John A., Rule, Anna M., and Madden, Bernard: The Chemotherapy and Serum Therapy of Pneumococcus and Streptococcus Meningitis. VI. The Cerebral-Cisternal Spine Lavage Method of Treatment for Septic Meningitis, Arch. Otolaryng. **9**: 429, 1929.
26. Idem: VII. The Intracarotid Treatment for Experimental Pneumococcus Meningitis, Arch. Otolaryng. **9**: 509, 1929.
27. Kolmer, J. A.: Intracarotid Method of Treatment for Meningitis With Recoveries, J. A. M. A. **96**: 1358, 1931.
28. McMahon: Quoted by Ersner and Mendell.
29. Crawford, A. S.: Intracarotid Treatment of Meningitis Experiences With Pregl's Solution of Iodine: Further Report, J. A. M. A. **98**: 1531, 1932.
30. Ersner, M. S., and Mendell, T. H.: Streptococcus Meningitis With Intracarotid Treatment and Recovery; Report of 2 Cases, J. A. M. A. **99**: 1596, 1932.

GRAVITY DRAINAGE OF INFLAMMATORY EDEMA

A Method for Elevation of an Extremity

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IN AN editorial in this Journal, Wangensteen[1] has discussed the role of immobilization and posture in the treatment of acute infections of the extremities. He concludes as follows: "Clinical trial suggests that immobilization and elevation are adjunct measures of distinct value in supporting the natural defense mechanism of the body in pyogenic infections of the extremities. Their use appears to rest on a rational physiologic basis."

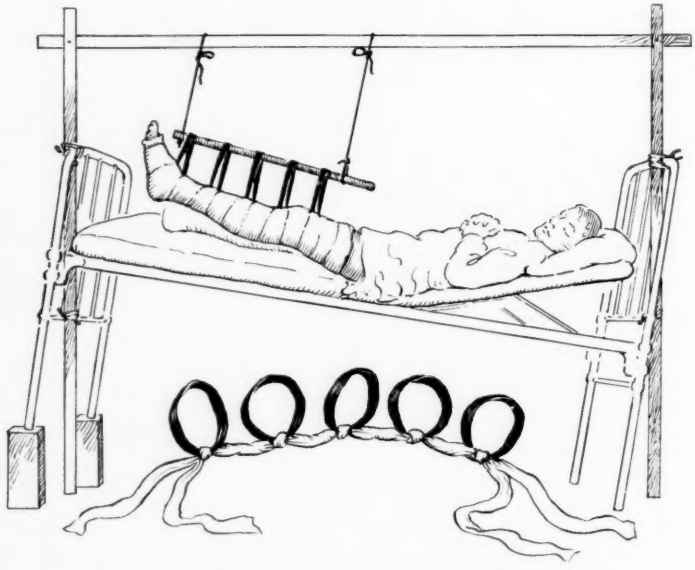

Fig. 1.—The foot of the bed is elevated on 10-inch blocks and the limb hangs suspended from the broomstick passing through the rubber rings. Insert shows method of fastening rings together.

I have had two years' experience with a method of elevation which has pleased me very much. The extremity hangs suspended at the desired elevation. The patient can move the limb and can change his position in bed without pain, and without disarranging the elevation.

The foot of the bed is put up on 10-inch blocks. The wound is dressed and the limb wrapped with 6 inch wide strips of bath toweling from the toes to midthigh. A large sterile bath towel, folded lengthwise, is laid along the under surface of the limb. Five rubber rings, made by cutting cross sections from an automobile inner tube, are tied together.

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One end is attached to the foot over the ankle and the other end above the knee. A snug bandage is applied, incorporating the rubber rings. A broomstick, hanging from an overhead frame, is passed through the rings and the leg suspended.

The arm can be suspended in a similar fashion but the elbow and wrist should be splinted on the under surface.

In acute infections which have not yet localized, the dressings should be changed daily and the limb gently inspected for abscess localization, which would require incision.

Limbs with plaster casts can be suspended with comfort to the patient. I have also used the method in terminal care of carcinoma of the breast with elephantiasis of the arm.

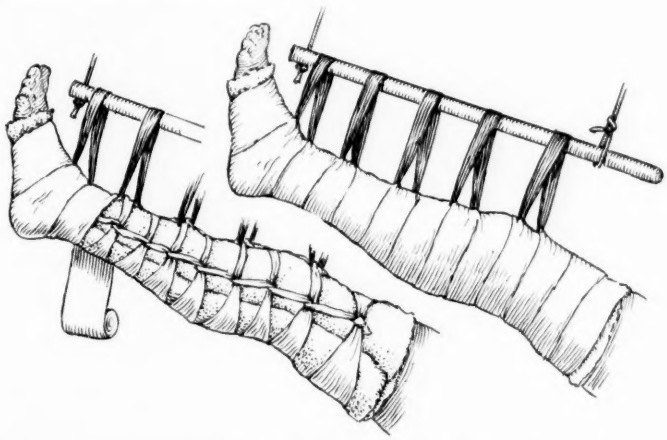

Fig. 2.—Showing method of attaching the rubber rings to the limb with bandages. Note that bowline loop in end of rope permits broomstick to be slipped out without untying.

The method was originally developed for the preoperative removal of lymphedema in elephantiasis of the leg. The patient can slip out the broomstick, walk to the bathroom, and on return replace the leg as it was. After Kondoleon operation, the limb is kept suspended until wound healing is complete.

REFERENCE

1. Wangensteen, O. H.: Anti- or Prophlogistic Treatment of Acute Infections? The Role of Immobilization and Elevation in Pyogenic Infections of the Extremities, SURGERY 4: 140, 1938.

AN ELASTIC BANDAGE BOOT FOR VARICOSE VEINS

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WITH varicose veins that are giving symptoms, there is always some swelling of the leg due to venous and lymph stasis. Firm elastic bandaging removes this circulatory stasis, gives comfort, and relieves pain.

The bandage commonly used for varicose veins is the cotton crepe bandage of elastic weave. The physician applies the bandage the first time it is used and then relies upon the patient to change it thereafter. This is rarely satisfactory as the patient does not apply it tightly enough; it loosens, drops down, and is ineffective. Gelatin boots, elastic adhesive strapping, etc., succeed where the crepe bandage fails, because they are applied and changed by the doctor.

However, the crepe bandage can be made into a bandage boot by the simple device of gluing the laps of the bandage together. This bandage boot has the good points of the gelatin boot and the elastic adhesive strapping, and yet is more comfortable to wear, easier to apply, and less costly.

The bandage boot is applied as follows: The leg is first bandaged with 6-inch-wide strips of heavy Turkish bath toweling made by cutting up a towel. The toweling should cover the dorsum of the foot and the heel and extend well up over the head of the fibula and the medial condyle of the tibia. The heads of the metatarsals should not be covered as this would prevent the wearing of a shoe.

A line of ordinary dextrin syrup (karo) is dabbed on the toweling along the crest of the tibia. A strip of thin splint wood ¾ inch wide and 8 or 10 inches long, with thumbtacks pushed through it at 3- or 4-inch intervals, is placed along the fibula, points outward. Over this is applied the crepe bandage (4 inches by 5 yards). A margin of the bath toweling is left exposed above and below to prevent chafing. The crepe bandage is applied smoothly and as tightly as possible. The syrup soaks into the toweling and the crepe bandage. It is dried by the body heat of the leg and firmly glues the two together into a bandage boot. The bandage is impaled on the points of the thumbtacks in the splint and cannot slide down. If the points protrude too far, they may be pushed back a little.

If the patient is a working man, an outside muslin bandage is applied for him to change when soiled.

Immediately after the bandage is applied, the toes are cyanotic and the patient complains that the bandage is too tight. But after walking

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about for a few minutes, the cyanosis clears up and the boot becomes comfortable. It is explained to the patient that walking favors venous circulation and he is encouraged to walk a good distance each day.

With the toweling underneath, it is virtually impossible to apply the bandage too tightly. The toweling acts as a padding and prevents bandage marks on the skin. Its resilience greatly increases the elastic compressive action of the bandage. It is porous and absorbent and prevents skin maceration and itching.

After wearing the boot a few days, the patient returns with the tissues much softer and less painful and with most of the edema gone. The veins are more clearly seen and palpated, and injection treatment is simplified. It is very useful in legs with painful brawny edema and ulceration, for its application secures immediate symptomatic relief and one may await the subsidence of the inflammation before attacking the

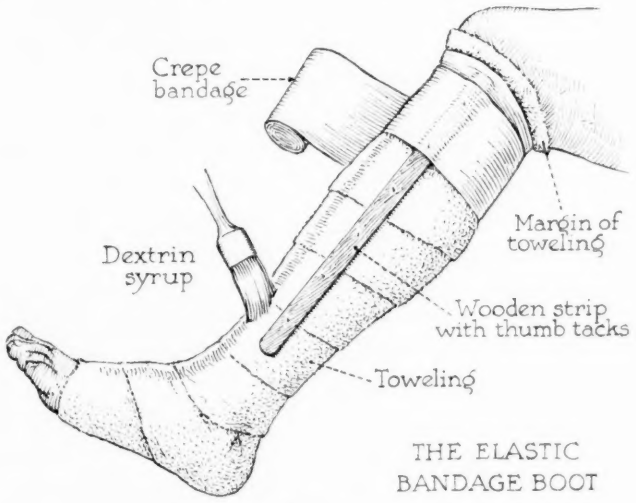

Fig. 1.

veins. After sclerosing injections, the boot is applied and remains in place until the next visit of the patient. In acute thrombophlebitis or after high saphenous ligation, the boot may extend up the limb to the groin if it is desirable. The bandage boot is also very useful in mild elephantiasis of the leg and may be left on for two, four, or six weeks as required.

SUMMARY

The ordinary crepe bandage which is commonly used to bandage legs having varicose veins can be made into an efficient bandage boot by wrapping the leg with a strip of bath toweling before applying the bandage and by gluing the two together with dextrin syrup.

Editorial

The Responsibility of the Surgeon for Postoperative Complications

MODERN SURGERY began when anesthesia and asepsis had become established. Before this time the pain of the ordeal or the almost inevitable sepsis which followed every operation restricted surgical therapy to a few serious and painful conditions. It was only natural that what we now look upon as postoperative complications and not a part of the original disease should have been lost sight of in the terror of the ordeal itself.

With the advent of modern surgery arose the field of elective surgery, for now it was possible to remove painlessly and with safety diseased organs from patients otherwise in good health. But again surgery was shown to be a mixed blessing. Just as when in the days following the discovery of anesthesia postoperative sepsis halted all surgical advance, so now serious and often fatal complications were noticed even in "clean" cases where the wound healed per primam. Patients died of pulmonary complications, and coma, anuria, and tetany followed certain procedures. From this time to the present an unremitting study of the causes of such complications has gone forward. Slowly but surely the surgeon has learned the risks of surgical therapy, and he now understands the incalculable benefits of proper preparation of his patient. Careful studies have revealed that certain disorders, which now can be appreciated by simple biochemical tests, will give rise to serious complications unless they are adjusted preceding the surgical procedure. Other studies have made it clear that the frequency and severity of pulmonary complications vary with the site of the operation and the type of technical surgery practiced.

These studies have given rise to the conscientious attitude of the modern surgeon whose energies are directed quite as much to a complete appraisal of the general condition of his patient and to measures calculated to improve the "risk" as to the treatment of the condition from which the patient suffers. To begin with, a more reasonable preparation of the patient arose through a better appreciation of the chemical and physiologic changes that occurred when surgery was attempted. Forty years ago it was the rule to starve, purge, and withhold water as preoperative routine. Now we have learned that perhaps the best preparation is that one which disturbs the patient as little as possible from his normal ways of diet, of exercise, and of living. Moreover, surgeons have noted that the patient hurriedly brought from an active life to the operating table because of trauma or intra-abdominal acute dis-

order, as with rupture of a duodenal ulcer, is not likely to have serious postoperative complications. To emphasize this point we have only to consider the seriously toxic thyroid patient. Every surgeon who does thyroid surgery takes care lest his patient be disturbed the morning of the operation. On the other hand, if we happen to have a healthy young boy with a hernia, he is often awakened early, his teeth given a special scrubbing, he is given a bath and sometimes an enema—a considerable ordeal to the unpracticed—all before he goes to the operating room. It is obvious that we still have to untie ourselves from many customs imposed by a preceding generation of surgical thinking!

When we consider postoperative sequelae we can say that much has been accomplished. There is both experimental and statistical evidence that the various pulmonary complications occur under all forms of anesthesia, including infiltration anesthesia and spinal anesthesia. From this we may broadly deduce that the anesthetic per se is not the essential responsible factor which gives rise to these unfortunate pulmonary complications. And yet one hears constant criticism of anesthetists and anesthetics. Furthermore when infectious lesions spread or when new infection is introduced at the operation, there is a constant tendency to speak of the diminished resistance of the patient or to blame the catgut or to say that the house staff suffered from "colds."

It has long appeared that this point of view has the unfortunate and serious aspect that it represents an attempt of the surgeon to search outside of the patient for the cause of the sequelae. Obviously no single factor extraneous to the patient is present in every case. The temperature of the operating rooms, the kind of anesthesia, "colds" among the assistants, and the type of surgery are all variable conditions. But we have in the wound itself, made by the surgeon, a single, always present source of trouble! It is obvious that in every surgical operation thrombi form where vessels are cut. These thrombi may be larger in those cases where there is unnecessary trauma, where tissues are roughly handled, and where desiccation is allowed to occur. Such thrombi are more apt to be of large size if vessels have been clamped and the ties put on distal to the clamped area so that injured intima and slowed circulation, chief factors in thrombosis, are present. Such thrombi, if they slip off, produce infarction with inevitable peripheral morbidity.

Every surgeon of experience appreciates the grave danger of surgery in certain infectious lesions, as, for example, carbuncles about the lip. Why is it that the lessons learned in this field cannot be applied elsewhere? In the surgical care of infection, whether it be a furuncle, a subcecal appendix, or an abscess of the brain or of the lung, the same desiderata are called for; that is, that the opening be made in the part nearest to the lesion so that a minimum of uninvolved tissue will be cut. When the lesion is superficial, the opening should be made in the center of the inflamed area so that the walling-off process which nature throws

about each infection may protect the patient from a spreading process. Think how often the scalpel is swept across an infected area and then out into a fresh and heretofore uncontaminated and therefore unprotected field! And consider this in relation to the common operation of appendectomy. It is unhappily the habit of some surgeons to utilize the same incision always for appendectomy. If a right rectus incision is always employed, the abdominal cavity will be opened in a certain number of people who have retrocecal appendicitis with abscess, and the abscess may be broken into from the side of the free and heretofore uninfected peritoneal cavity in order to secure drainage. This means contamination of the abdominal cavity; whereas, a posterior, muscle-splitting incision in the flank would have avoided opening the abdominal cavity. It is unfortunate that the lessons learned in the bacteriologic laboratory are not more intimately applied in the clinic!

When we consider the occurrence of new wound infection, we must consider the suture material, or the dry goods that come out of our autoclaves, or finally the treatment of the tissues themselves. In the first place, catgut and kangaroo tendon material can never be considered absolutely aseptic. In the next place the autoclaves in every hospital must be constantly and scrupulously checked for adequate performance. The surgeon cannot delegate this responsibility entirely to the nurse or the hospital administration. If he himself has insufficient knowledge of how to do this, he should call in experts to assist him. Finally we must accept the fact that every wound receives contamination from the skin and air bacteria. The deeper layers of the skin cannot be sterilized. The circulating air always contains bacteria, though they can be somewhat reduced by the expensive process of washing the air and perhaps by the use of infrared rays in the operating room. The question is, can the body care for the number of bacteria which inevitably will be introduced? This we know will depend upon what has gone on in the wound. If the tissues have been allowed to dry, if there has been rough handling so that many cells are dead or are dying, if great tabs of tissue have been strangulated by gross ligature material so that they have lost their blood supply and are to undergo necrosis, the few bacteria introduced may cause dissolution of the wound, breaking down of the healing process, and suppuration.

All of the considerations above should direct the attention of the surgeon to the fact that the one thing common to every operation is the wound. If his technical performance is carried out with gentleness and with high regard for the life of each individual cell, then at least some of the unfortunate postoperative sequelae will disappear.

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Recent Advances in Surgery

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HEPARIN: A REVIEW OF ITS HISTORY, CHEMISTRY, PHYSIOLOGY AND CLINICAL APPLICATIONS

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INTRODUCTION

DURING the past few years rapid progress has been made in the problem of preparing heparin suitable for clinical use. This substance now can be purified to such a degree that it may be introduced into man without fear of any untoward effects other than those which may arise consequent upon rendering the circulating blood incoagulable. At present pure heparin is a relatively expensive product, a factor which may retard considerably developments in its therapeutic application; however, the recent advances in knowledge of its chemical structure offer the hope that in the near future heparin itself, or equally active and useful synthetic compounds of similar structure, will become available at more moderate costs.

The clinical possibilities of a nontoxic anticoagulant are numerous, and a considerable literature on this subject has arisen. It has seemed well, therefore, to attempt to summarize some of the existing information concerning heparin from several points of view. It is the purpose of this review to discuss briefly its history, chemistry, mechanism of action, and recent physiologic and clinical investigations involving its use.

HISTORY

The first recorded observations of the anticoagulant properties of heparin were those made by McLean[1] in Howell's laboratory while studying the thromboplastic behavior of several phosphatides. Two were found to inhibit clotting: *cuorin*, prepared from heart muscle by the method of Erlandsen,[2] and the *heparphosphatid* of Baskoff,[3] isolated from dog liver. Shortly afterward Howell and Holt[4] made an extensive study of heparphosphatid. They observed that although the cuorin prepared by McLean was identical with that of Erlandsen, the heparphosphatid he had isolated differed somewhat in its properties and nitrogen-phosphorus ratio from the original preparation of Baskoff.

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For the heparphosphatid with which they were dealing, Howell and Holt proposed the name "heparin" to indicate its origin in liver, and they described in detail the procedure they used in its preparation free from cephalin. The acetone precipitate of the ether soluble fraction of dried dog liver was repeatedly precipitated from alcohol at 50° C. until it began to lose its solubility in anhydrous ether. It was then taken up in chloroform and precipitated twice from warm alcohol. The final product when dried and pulverized was a chocolate powder, water soluble, heat stable, and had a nitrogen-phosphorus ratio of 2.5:1. One hundred milligrams per 100 c.c. shed blood completely inhibited clotting, and intravenous injections of 100 mg. per kilogram into dogs greatly increased the clotting time of subsequently drawn blood. The effect wore off in three to four hours. No changes were observed in blood pressure, heart rate, respiratory rhythm, or rectal temperature in these experiments, nor in those of Reed.[5] From experimental evidence it was concluded that heparin had two effects upon the coagulating system: (1) it inhibited the activation of prothrombin to thrombin by calcium, by reacting in some way with prothrombin; and (2) it was an activator for "proantithrombin" permitting the conversion of this postulated substance into antithrombin. While admitting there was no direct evidence that heparin occurs normally in blood, these authors believed the indirect evidence favored the hypothesis that both heparin and proantithrombin are physiologic constituents.

In 1923 Howell[6] published an alternative method of preparation that yielded a more active crude product, which was further purified[7] by employing taka diastase to destroy accompanying glycogen, boiling, methyl alcohol to precipitate any protein, and cadmium chloride to eliminate other undefined contaminants. One gram of crude heparin yielded 18 to 20 mg. of the purer substance, 1 mg. of which prevented the coagulation of 40 c.c. of cat blood. Further purification[8] was obtained by precipitation as the barium salt, which when freed of barium and dried was an almost colorless, scaly material, water soluble and heat stable, 1 mg. sufficing to keep 100 c.c. of blood liquid. The absence of phosphorus in this preparation forced the conclusion that the active substance was not a phosphatide, and that previous positive tests for this element were due to contaminants. The reactions of this purer heparin in the blood coagulation system were the same as those of crude heparin.

Using the action on proantithrombin and the anticoagulating activity as tests, heparin was demonstrated in (1) the plasma of dogs in peptone shock (moderate quantities) and (2) normal dog plasma (minute quantities). In establishing anticoagulating activity of the plasma, the contained heparin was concentrated by a brief procedure consonant with obtaining crude heparin. After clotting had taken

place heparin could no longer be demonstrated in plasma. Its normal anticoagulating influence was presumed to be neutralized by cephalin liberated in shed blood.[7]

Shortly following the isolation of crude heparin by Howell and Holt, the firm of Hynson, Westcott, and Dunning (Baltimore) undertook its production for general physiologic use. The preparations since available from several American and European firms have had potencies (purities) ranging from that of crude heparin to the 1925 product of Howell. Only very recently has the chemically pure substance been obtainable, in consequence of the investigations of Schmidt and Fischer, Charles and Scott, Bergström, and Jorpes, whose work will be considered in the section dealing with the chemistry of heparin.

Studies of the mechanism of action, physiologic and chemical properties, and possible clinical application of heparin paralleled progress in its purification. These will be discussed in appropriate sections subsequently.

MECHANISM OF HEPARIN ACTION

The controversies over the mechanisms involved in blood coagulation which have arisen in the past forty years are outside the scope of this review and have been dealt with adequately elsewhere.[9-17] It may be stated unequivocally that the problem has not been solved nor are any of the prevalent theories consistent with all experimentally confirmed facts. Only a portion of that literature directly concerned with the behavior of heparin will be considered.

Inasmuch as heparin is intimately concerned with the Howell theory, it is convenient to discuss it from that standpoint. The Howell hypothesis may be briefly stated as follows:

There are present in circulating blood prothrombin, calcium ions, fibrinogen, antithrombin, antiprothrombin (heparin) and an antithrombin precursor (proantithrombin). The antiprothrombin (heparin) has the function (1) of stabilizing prothrombin by combination with it, and (2) of promoting the production of antithrombin from its precursor, proantithrombin. (At any rate the latter action is claimed for heparin *added* to plasma.)

In shed blood, thromboplastic substance (cephalin) liberated from injured tissues or platelets combines with antiprothrombin (heparin). The unstable prothrombin reacts with calcium ions forming thrombin, which, when in excess of the antithrombin, permits the conversion of fibrinogen to fibrin.

Explicit functions, therefore, are assigned to heparin. These are (1) that it acts as an antiprothrombin and (2) that it stimulates the production of antithrombin by activation of a precursor (proantithrombin[4, 7]). Implicit to this theory is the presence of heparin in blood as a physiologic constituent, necessary for the maintenance of its fluidity.

The double action of heparin seemed well substantiated by the original observations of Howell. In addition prothrombin is now believed by many to be identical with complement "mittel-stuck,"[18] and heparin has an inhibitory action on this component of complement.[18, 19] The claim for its occurrence as a physiologic constituent of blood has been supported by several lines of evidence: (1) It is a substance which can be isolated from a number of tissues other than liver and lung;[20-22] (2) by similar methods of isolation, a substance with identical properties may be isolated (a) from normal plasma in minute quantities, and (b) from the incoagulable plasma of the peptonized dog in larger amounts, but (c) none is to be obtained from the serum of clotted blood;[7] (3) protamine forms an insoluble inactive complex with heparin in vitro, and also effectively diminishes clotting time of shed blood either by addition in vitro or by previous intravenous administration;[23, 24] (4) mucoproteins, containing mucoitinsulfuric acid, have a wide physiologic distribution and are particularly rich in the Ehrlich mast cells in areolar connective tissue,[21, 22] the granules of which contain mucoitinpolysulfuric ester, i.e., heparin (vide infra).

In spite of the attractiveness of the Howell concept of heparin function, there is considerable evidence against it. The assumption, by practically all investigators interested in heparin from points of view other than its mechanism of action, that it functions as an antiprothrombin is not justified at the present time. Mellanby[25] and Quick[26-28] have made it appear more than likely that heparin does not act as an antiprothrombin but exclusively as an antithrombin (Mellanby) or as an activator to an antithrombin precursor which is albumin (Quick). The latter prepared purified prothrombin by Eagle's method[29] and showed that upon addition of calcium chloride, thrombin was formed readily and in the same amounts in the presence or absence of added heparin. Also heparin was found not to inhibit the action of thrombin on fibrinogen which had been isolated by sodium chloride precipitation, thus refuting Mellanby and strengthening part of Howell's earlier interpretation that addition of heparin produced an antithrombin from some precursor. Finally, it was shown that the coagulation time of oxalated plasma as well as purified fibrinogen is inversely proportional to the concentration of thrombin, a straight line relationship which would not hold if appreciable amounts of antithrombin were present, and which is disturbed by the addition of minute amounts of heparin. This is interpreted as indicative of the absence of antithrombin, and, accordingly, heparin in normal blood.

Against the conception that heparin enters into combination with prothrombin is the observation that certain proteolytic enzymes change prothrombin to thrombin,[30] although here it may be possible that these enzymes split off heparin as well as directly attack prothrombin.

It is difficult to reconcile with the work of Clowes[31] the assumption that cephalin (thromboplastic substance, tissue extract, platelets) liberates prothrombin by entering into chemical or physical combination with the stabilizing heparin. This investigator added cephalin to citrated plasma, passed the mixture through a Berkefeld filter which retained the lipoid, and then found the filtrate did not promptly coagulate upon recalcification unless additional cephalin was added.

Directly opposing the implications of this observation are the investigations of Fischer[32, 33] which indicate (1) that thromboplastic material rapidly removes heparin from solution and (2) that this reaction is a stoichiometric one forming a dissociable complex.

Not a few investigators, e.g., Eagle,[34] indicate that a case can be made for heparin being an artificial substance produced by tissue manipulation, and that the isolated product may in no way be related to the physiologically circulating anticoagulant, if, indeed, there be such. This appears extreme in view of the facts which will be considered in discussing its chemistry. It would seem that in light of the existing differences of opinion, a temporarily safe position regarding the role of heparin might be stated as follows.

Heparin is probably, but not certainly, the normal circulating anticoagulant assisting in or necessary to the maintenance of the fluid state of the blood. Its anticoagulant action is effected largely through its power to activate a precursor to antithrombin rather than by any combination with prothrombin which renders the latter insensitive to thromboplastic substance and calcium ions. Although under certain conditions heparin and thromboplastic substance may enter into combination to "neutralize" one another, the coagulating activity of the latter is largely due to the increase in thrombin caused by its action on prothrombin.

It is realized that such a conception is entirely unsatisfactory and represents merely one point of view that may be gained from the literature on this vexed subject. The unhappy state of the problem of the nature and action of the physiologic anticoagulant is emphasized by the excellent discussions of Eagle.[34, 35]

THE CHEMISTRY OF HEPARIN

The literature on the chemistry of heparin may be divided into two categories: that dealing with (1) its isolation, identification, and probable structure, and (2) its chemical properties in vitro. For convenience the first category will be dealt with chronologically.

The Isolation, Identification, and Probable Structure of Heparin.— The early observations on the chemical properties of heparin were made by Howell who followed his isolation of crude heparin[4] by further purification[6, 7] and finally prepared a product with an activity of 100 units per milligram.[8] (For comparison, "pure" heparin is now conceded

an activity of approximately 500 Howell cat units* per milligram, the insoluble brucine salt fraction being somewhat higher (vide infra). The following observations were made by Howell on this product: phosphorus and nitrogen, negative; no reduction of Fehling's solution until after hydrolysis; no color with iodine (glycogen test); α-naphthol reaction (Molisch) positive; test for glycuronic acid (Tollen's naphthoresorcinol and Bial's orcinol reagents) positive; hydrolysis with dilute hydrochloric acid destroyed its anticoagulant activity giving a water soluble residue behaving like glycuronic acid; boiling with dilute nitric acid, and evaporation left a sticky residue mixed with an inorganic crystalline deposit containing calcium and sulfur; ash, 37 per cent.

It was concluded that heparin was probably a glycuronic acid derivative or condensation product containing, as isolated, calcium and sulfuric acid in the molecule. In support of this it was found that glycuronic acid heated to 250° formed a dark-colored water soluble condensation product which had an anticoagulating activity of one to two units per milligram.

In 1933 Schmitz and Fischer,[36] starting with a Kahlbaum preparation of heparin, succeeded in preparing a crystalline brucine salt which had thirty-two times the anticoagulant activity of the original material. The method of assay had been previously described by them,[37] and cannot be compared directly to that of Howell; however, it may be presumed, in light of later developments, that this product had the same order of activity as pure heparin, which, indeed, it seems to have been except, probably, for a small amount of ash resulting from the binding of cations by the acidic groups.[38] After removal of phosphate by magnesia mixture, they adsorbed the active material on silica gel, and after elution, prepared two lead salts, one of which contained the active substance. After removal of the lead, a barium salt was precipitated from which, in turn, a brucine derivative was made. The formula assigned to the free acid was $C_{18}H_{32}O_{17}.6H_2O$. Incinerating the barium salt in sulfuric acid yielded only traces of ash other than barium sulfate, but neither the free acid nor the brucine salt was entirely ash-free, and they ascribed this to the ability of heparin to bind salts, stating that the ash content, hence the composition of heparin, changes with the mode of preparation. In their opinion pure heparin should be considered ash-free.

In a subsequent paper[39] they stated that heparin is probably a carbohydrate compound with a molecular weight of about 650, containing one free carboxyl group. The Molisch and naphthoresorcinol tests were positive, but there was no reducing activity until after acid hydrolysis, which suggested the presence of an uronic acid with a

*A Howell cat unit is that degree of anticoagulant activity required to inhibit clotting of 1 c.c. of cold cat's blood for twenty-four hours.

blocked aldehyde group. No nitrogen was reported, but the high barium content of the barium salt was remarked upon. It was thought this was due to salt binding power rather than to heparin acting simply as an anion.

Almost simultaneously, the findings of Charles and Scott appeared in three important papers. The first[40] dealt with the large scale preparation of crude heparin from beef liver. For details of this procedure, which differs considerably from Howell's, the original description should be consulted. The second[20] concerned the distribution of heparin in various tissues determined by the quantities which could be extracted from them. In the ox it was found that liver, muscle, and lung yielded comparable amounts, the latter tissue being richest. Much smaller quantities were obtained from heart, thymus, spleen, and blood. Only negligible amounts were recovered from serum. Dog liver contained about twice as much as that of the ox. The third paper[41] dealt with the purification of crude heparin. Upon a preliminary, partially purified product several important observations were made. It contained 3.2 per cent nitrogen and the activity was destroyed by treatment with nitrous acid, indicating that heparin contained a free amino group which was concerned in its anticoagulant action. It was stable to oxidizing and reducing agents. In alcohol the ammonium salt was soluble, whereas the sodium salt was insoluble, suggesting the formation of definite salts, and the presence of a carboxyl group.

The purification of crude heparin involved considerable manipulation (see original) including removal of inactive material by Lloyd's reagent, cadmium chloride, hydrogen peroxide, and fractional precipitation with sodium chloride and acetone, during which calcium found present was removed by oxalate. Three products were prepared: (1) free heparin, (2) the sodium salt, and (3) the hydrochloride, the latter being microcrystalline, and by analysis found to be 22 per cent carbon, 37 per cent hydrogen, 27 per cent nitrogen, and 33.3 per cent ash. The other two products had nearly the same composition. The ash was stated to consist mainly of sodium chloride. The Molisch test was positive and the iodine test for glycogen negative. Contrary to Howell and Schmitz and Fischer, the orcinol, phloroglucinol and naphthoresorcinol tests were negative even in 4 per cent concentrations. The activity of the three preparations was 421, 484, and 471 Howell cat units respectively, with an average of 459. The details of the method of assay were given.

It is seen, therefore, that at this time (1933) there was no general agreement as to either the chemical properties or composition of purified heparin. The first communication of Jorpes[42] did much to clarify this subject. After preparation of crude heparin according to the method of Charles and Scott, followed by partial purification by treat-

ments with Lloyd's reagent, he subjected the samples to analysis. The ash varied from 38 to 41 per cent, and nitrogen from 1.6 to 1.8 per cent. Quantitative estimation of hexuronic acid indicated 17 to 19 per cent was present, and another analysis for hexosamine yielded 12 to 14 per cent. A test for ester sulfate was positive as was that for N-acetyl. This analysis was so completely in agreement with what might be anticipated for chondroitinsulfuric acid that it seemed unlikely it could be anything else; however, chondroitinsulfuric acid was devoid of anticoagulating activity. The ash content was more carefully investigated, and about 7.5 per cent sulfur as ester sulfate was shown by electrodialysis. As chondroitinsulfuric acid contains only about 3 per cent sulfur, and as there were reasons to believe the extra ester sulfate was fixed to the chondroitin, the presumption of a chondroitinpolysulfuric acid seemed plausible. The observed ratio of ester sulfate to chondroitin by analysis was about 2.5:1 which could be explained by the presence of a mixture of chondroitintrisulfuric and chondroitindisulfuric acids in about equimolecular proportions.

Study of the properties of heparin and chondroitinsulfuric acid revealed certain important differences. The barium salt of heparin readily flocculates whereas that of chondroitinsulfuric acid is soluble; likewise heparin but not chondroitinsulfuric acid is flocculated in cold methyl alcohol by brucine. Freed from brucine this precipitate analyzed as calculated for chondroitintrisulfuric acid. In addition the quinine salt was prepared from a neutral solution of heparin and after removal of the quinine, the residue had a composition agreeing with chondroitintrisulfuric acid. Finally, in order to obtain a pure brucine salt, the metallic cations of the heparin samples as well as traces of free sulfates, were removed by electrodialysis and the brucine salt precipitated in methyl alcohol. This salt had the composition approximating chondroitintrisulfuric acid, whereas the material recovered from the mother liquor contained sulfur in proportions somewhat below that calculated for chondroitindisulfuric acid.

The observation was also made that the acetic acid recoverable from heparin diminished in the final products. As these preparations maintained their anticoagulating activity it was believed the acetyl group had been split during manipulation, and that it was unessential to the anticoagulant effect. The probable importance of the ester sulfate grouping was emphasized by pointing out that almost all substances known to inhibit blood clotting effectively are high molecular weight sulfonic or sulfuric acid derivatives (liquoid, germanin, pontamine pink, chlorazol sky blue, and numerous other dyes).

The assays of the presumed chondroitintrisulfuric acid were made by a method which cannot be directly compared with that of Charles and Scott, except in two instances where the partially purified heparin prior to precipitation with brucine was assayed at about 500 Howell

cat units per milligram; however it is likely the actual activity at this stage was about half this value.[43] The naphthoresorcinol test was negative, in confirmation of Charles and Scott, but differences in technique may have explained the opposite findings of Howell, and Schmitz and Fischer.[38]

It would appear, then, that Jorpes was dealing with essentially the same substance which had been prepared by Schmitz and Fischer and by Charles and Scott, and which was the active ingredient of Howell's best product. The latter workers had not fully appreciated the significance of the ash content and in addition Schmitz and Fischer had failed to observe the presence of nitrogen. Jorpes' quantitative observations on ester sulfates, hexuronic acid, glycuronic acid, and N-acetyl definitely pointed to the class of compounds with which heparin must be identified and did much to explain the discrepancies other investigators had encountered in respect to the ash. (It is to be remembered that a free ester sulfuric acid would yield no ash, whereas any metallic salt of such a compound would give an ash composed of the corresponding sulfate. In the preparation of purified heparin the procedures entailed offered the possibility of the formation of metallic salts in every instance, some of which were not fully resolved by further treatment, e.g., in preparation of the hydrochloride or the brucine salt.) It was concluded that the organic material in heparin is chondroitin, and that the active anticoagulant is a chondroitinpolysulfuric acid or a mixture of these acids.

Schmitz[44] doubted this to be the case stating in a brief communication that he had prepared an extremely active heparin with an ash content of about 5 per cent, containing no sulfuric acid. Not doubting Jorpes' actual observations, he suggested that either a series of anticoagulants occur in tissues, or that derivatives of the active compound are formed during manipulation, this explaining various divergent results. Details of the testing for presence of sulfate were not given, and it is difficult to escape the conclusion that its apparent absence was an error of observation. The status of the heparin problem at this time was summarized by Jorpes.[45]

In a later paper Charles and Scott[43] report further efforts to isolate heparin in a pure form. By preparing lung heparin as the calcium salt, they were able to remove the calcium with oxalate, and reduce the ash content to 5 per cent. Then taking advantage of the fact that benzidine forms an amorphous precipitate with heparin, this derivative was prepared which, freed of benzidine and recrystallized from ether and glacial acetic acid, yielded a product with only 0.7 per cent ash. From this the barium salt was readily prepared in a crystalline form. The ash in this amounted to 33.5 per cent, the total sulfur in the crystals being 9.3 per cent and the amino nitrogen 0.4 per cent. The barium could be removed by several reprecipitations with benzidine.

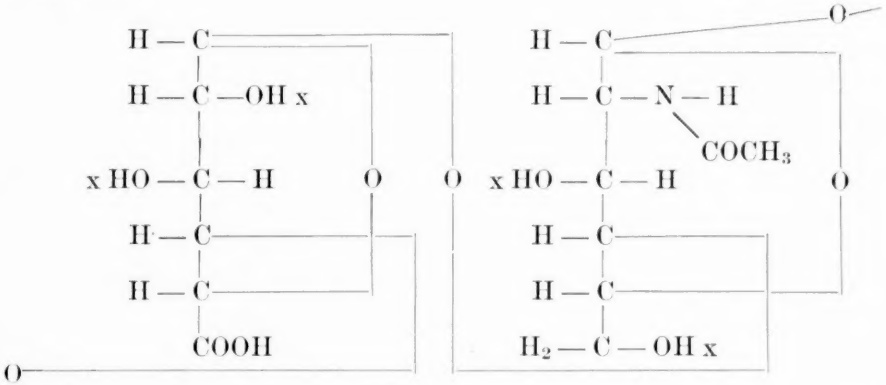
Calculations from analyses of the benzidine derivative gave the following composition for benzidine-free heparin: calcium, 23.1 per cent; hydrogen, 4.99 per cent; nitrogen, 2.1 per cent; sulfur, 11.54 per cent. The empirical formula assigned was $C_{25}H_{65}O_{50}N_2S_5$. This analysis did not support Jorpes' view that heparin is chondroitinpolysulfuric acid, the carbon content being much too low. The crystalline barium salt was inactivated by nitrous acid, formaldehyde, and prolonged exposure to acid alcohol which split off the ester sulfate groups. Its anticoagulant activity was found to be approximately 500 Howell cat units per milligram.

The work of Jorpes led Bergström[46] to investigate the heparin activity of several synthetic sulfuric acid esters of carbohydrates which he prepared by sulfonation. Glucose- and galactose-tetrasulfuric acids, and glucosamine-trisulfuric acid were inactive as were the esters of the corresponding polymers if hydrolyzed during sulfonation; however, the esters of the polysaccharides, cellulose, starch, glycogen, chitin, pectin, gum arabic, and chondroitin, had various degrees of anticoagulant activity. Chitindisulfuric, cellulose-trisulfuric, and pectin-polysulfuric acids were about one-tenth as active as Jorpes' purified presumed chondroitintrisulfuric acid, and the rest, other than synthetic chondroitintrisulfuric acid, were considerably weaker. The synthetic chondroitintrisulfuric acid had only about a fifth the activity of Jorpes' isolated product, a considerable discrepancy considering that by analysis the synthetic compound had between three and four moles of sulfate per mole chondroitin. It was nontoxic to rabbits, in contrast to the cellulose derivative.

The findings of Bergström were confirmed and extended by Chargaff et al.[47, 48] who found that anticoagulant activity was exhibited by polyvinylsulfuric acid, cellulosemono- and disulfuric acids, galactansulfuric acid and cerebroside sulfuric acids. None of these approached the activity of a partially purified heparin preparation, and they also observed a number of sulfuric and sulfonic derivatives which were inactive in spite of rather high molecular weight. They concluded that the following properties are necessary for inhibitor activity—water solubility, high molecular weight, and combined sulfuric acid, or perhaps other acids of similar strength. It is now evident that this generalization must be abandoned in favor of some more fundamental concept of the effect of charge, molecular weight, and chemical composition on the stability of proteins, e.g., Herrmann[49] finds certain basic dyes are strong anticoagulants. Similar observations have been made by others[50] employing simpler organic bases.

Recently Jorpes and Bergström[51] were able to show that the amino sugar in purified heparin is glucosamine, not galactosamine. The latter is characteristic for chondroitin, whereas the former is a component of the closely related mucoitin, a circumstance which forced the con-

clusion that heparin is to be considered a mucoitinpolysulfuric ester.[52, 38] The chemistry of chondroitinsulfuric and mucoitinsulfuric acids is briefly outlined by Harrow and Sherwin.[53] These substances are the prosthetic groups of the corresponding chondro- and mucoproteins. They consist of units of an hexuronic acid, presumably glycuronic, an amino sugar, sulfuric and acetic acids. The acetic acid is present as an N-acetyl group on the amino sugar, and sulfuric acid, one or more moles, is bound by an ester linkage to the free hydroxyl groups of the hexuronic acid and/or the hexosamine, the latter being galactosamine in chondroitinsulfuric acid and glucosamine in mucoitinsulfuric acid. Removal of the sulfuric acid from these compounds yields chondroitin and mucoitin, respectively. These units are probably bound to one another through the usual carbohydrate ether linkages to form chains, thus yielding a substituted polysaccharide analogous to glycogen, starch, cellulose, chitin, etc. The structure of a unit of mucoitin is shown in the accompanying structural formula,[52, 54] the points where esterification with sulfuric acid may take place being designated by *x*.



Jorpes and Bergström[52] studied the hydrolysis rates of heparin and chondroitinsulfuric acid. It was found that the heparin prepared from the insoluble brucine salt showed a much slower hydrolysis rate than that of the soluble brucine salt, the rate of the latter approaching that of chondroitinsulfuric acid. The most highly esterified heparin is, therefore, most stable. Liver and lung heparin were found to be identical except that the proportion of highly esterified heparin in the latter is smaller, and the anticoagulating activity correspondingly lower. The amino sugar of lung heparin was also found to be glucosamine.

It was noted that the amino group in the purest heparin samples is not free, yielding no nitrogen with nitrous acid. Although the evidence is good that it is blocked by an acetyl group, only about half of the theoretical acetic acid could be recovered by measures instituted for its isolation. The hexuronate appears to be glycuronic acid, but saccharic acid was not demonstrated upon oxidation. They concluded

that heparin was not a definite compound but a mucoitinpolysulfuric ester containing at least the trisulfuric and probably the mono- and disulfuric derivatives. The proportions of these determine the anticoagulant activity, the greater activity being associated with the higher sulfate content. Heparin from various tissues varies in the proportions of these derivatives, and hence in its activity, unless they are separated by the isolation procedures, e.g., by preparation of the insoluble brucine derivative.

Astrup and Jensen have recently described their methods of preparation[55] and purification[56] of heparin. Their purest product resembles that of Charles and Scott and has a carbon content somewhat low for mucoitinpolysulfuric ester. This difference would lose its significance were it to be shown that acetylation of the amino group was not constant in all units of the polymer. It is to be recalled that only about half of the theoretical quantity of acetic acid has been demonstrated by hydrolysis.

Strong support for the main contentions of Jorpes and his co-workers is to be found in the histologic investigations they have made of the distribution of heparin in tissues. Lison[57, 58] had shown that the metachromatic staining reaction given by mucoid and cartilaginous tissue with toluidine blue is due to the presence of mucoitin- and chondroitinsulfuric acids, and that the reaction is specific for these sulfuric acid esters of high molecular weight. When the reaction was tested on heparin solution it was found that as little as 1.5 mg. in a liter of 0.01 per cent dye gave a distinct metachromatic shade, and 3 mg. gave a strong violet color, a precipitate gradually forming. The color with heparin is about one hundred times more intense than with chondroitinsulfuric acid.[54] The reaction given by heparin is precisely that given in tissues by the granules of the mast cells of Ehrlich, and in a very important paper Holmgren and Wilander[21] exhaustively discussed the morphology, chemistry, and function of these cells, and their relation to the heparin problem. Their distribution was investigated further, using the toluidine-blue reaction and a special fixing technique to escape the difficulties consequent to the water solubility of the granules. Mast cells were found to have a wide distribution in the several species studied, being particularly rich in the connective tissue surrounding blood vessels. The distribution was consonant with the existing data concerning the relative richness of various organs as sources of heparin. The ester sulfate content of tissues was found to parallel its content in mast cells, as was the content of crude heparin. The morphologic and chemical observations all strongly support the conclusion that (1) the metachromatic granules in these cells contain heparin, (2) that the cells have secretory activity, and (3) that their function is to supply the circulation with the physiologic anticoagulant.

In a subsequent paper by Jorpes, Holmgren, and Wilander[22] the occurrence of mast cells and heparin in the blood vessel walls was further studied. Diffuse metachromasia was found in the walls of the great vessels, mast cells being especially rich in the vena cava, which might explain the delay in post-mortem clotting in it. The yields of heparin by extraction corresponded to the numbers of mast cells in these vessels. Large numbers of mast cells were found in the cornea and it was suggested that this might account for the absence of clotting when small hemorrhages occur in this region. The more general aspects of these findings, as well as a brief summary of some other phases of the physiology of heparin, were given in later communications by Jorpes.[54, 59]

In summary, then, it may be stated that the chief contentions of Jorpes and his co-workers regarding the chemistry of heparin appear to be correct. These may be briefly recapitulated as follows:

Heparin is not a definite chemical compound, but a mucoitinpolysulfuric ester of variable composition. The variables are (1) the number of sulfuric acid groups substituted into the individual mucoitin units, and (2) the positions into which they are substituted; (3) the degree of polymerization, i.e., the number of mucoitin sulfuric acid units which are linked together to form the polysaccharide structure, and (4) the relative esterification of each of the units so employed. The heparin preparations separated by chemical procedures have anticoagulant activities roughly proportional to the degree of esterification with sulfuric acid, the higher esters being the most active. The insoluble brucine derivative of heparin is composed largely of the higher esters, particularly mucoitintrisulfuric ester, and has an activity somewhat greater than 500 Howell cat units per milligram. Products isolated from various tissues may differ in activity due to differences in degree of esterification, and of polymerization until the chemical fractionation affords a separation of the identical components. Heparin is found in a large number of body tissues and is concentrated in the mast cells of Ehrlich where it may be identified by the metachromatic staining reaction with toluidine blue. The anatomic locations of these cells, in connective tissue around and in blood vessels, and their staining characteristics support the hypothesis that one of their functions is the elaboration and secretion of the physiologic anticoagulant.

For the moment we must consider as "pure heparin" any mixture of the various naturally occurring mucoitinpolysulfuric esters which have been freed of extraneous materials such as protein, accompanying salts, etc. It is seen that several of the products isolated by the various investigators mentioned above satisfy these criteria.

Chemical Properties of Heparin in Vitro.—The strong electronegative charge of heparin makes it an agent capable of exerting considerable influence on colloidal systems. Thus, Fischer[60] has shown that when

heparin is added to a neutral solution containing protein, the isoelectric point of the latter is shifted toward the acid side. Thus, in the case of globulin, the molecular combination with heparin is more stable on the alkaline side of the isoelectric point than before, and already precipitated globulin may be peptized by heparin addition. On the acid side of isoelectric point the protein is rendered less stable by heparin addition. This stabilizing effect of heparin in neutral solution is considered to be an important element in its anticoagulant action through prothrombin.[60, 61] The addition of heparin to albumin in weakly acid solution, and near its isoelectric point, produces flocculation, the insoluble complex being indistinguishable in several respects from globulin; in fact, this observation formed the basis of Fischer's theory that all the globulin fraction of serum arises from the action of antiprothrombin (heparin) on albumin.[62] That the heparin-albumin complex is actually globulin is generally denied, as it does not have the same solubility relationships in salt solutions as native globulin[63, 64] nor does its osmotic pressure,[65] molecular weight,[66] or immunologic behavior[67] differ from that of serum albumin, although it has lost the property of solubility at the isoelectric point.[68] The flocculating and peptizing action of heparin at certain hydrogen-ion concentrations has been confirmed, and forms the basis for Fischer's turbidity method of quantitative estimation of heparin. Fischer has shown that heparin and thromboplastic substance (cephalin) react stoichiometrically with the formation of a dissociable complex.[32] Schmitz and Kühl[69] found that the anticoagulant activity of heparin serum was quickly destroyed upon warming, and that even at room temperature inactivation rapidly occurred. Both the albumin and globulin fractions of serum were able to effect this when added to a buffer solution of the anticoagulant, presumably by the formation of some undefined complex. This is no doubt important in relation to the rapid return of the coagulation time to normal following intravenous injection of heparin.

Fischer and Schmitz[70] have also shown that heavy metals accelerate clotting in heparinized plasma, and attribute this to the formation of insoluble heavy metal salts of the anticoagulant. The silver ion is particularly effective in this respect. Various aspects of these properties of heparin have been summarized by Fischer and interpreted in terms of their relation to coagulation.[71]

The important observation that heparin and protamine combine chemically was made by Chargaff and Olson,[24] who found the anticoagulant effect of heparin to be abolished by protamine added in vitro, or administered intravenously. The nature of the heparin-protamine complex has been further studied by Chargaff,[72] who also found that protamine and cephalin likewise form an insoluble complex.[73] A part of the effect of protamine addition to blood containing

heparin may be due to simultaneous combination with thromboplastic substance. This might explain the failure of protamine to shorten the coagulation time of normal chicken plasma,[72] i.e., to demonstrate the presence of small amounts of heparin in normal blood.

The quantitative relations between heparin and protamine and heparin have been examined,[23] 0.3 mg. of the former being neutralized by 1 mg. of the latter in vivo or in vitro. Protamine, however, is toxic when administered intravenously to dogs, although not to guinea pigs.

The toluidine blue reaction given by heparin has already been mentioned.

(To be continued in the April issue. The additional references will accompany the second section.)

REFERENCES

1. McLean, J.: The Thromboplastic Action of Cephalin, Am. J. Physiol. **41:** 250, 1916.
2. Erlandsen, A.: Untersuchungen über die Lecithinartigen Substanzen des Myocardiums und der Quergestreiften Muskeln, Ztschr. f. physiol. Chem. **51:** 71, 1907.
3. Baskoff, A.: Über das Jecorin und andere Lecithinartige Produkte der Pferdleber, Ztschr. f. physiol. Chem. **57:** 395, 1908.
4. Howell, W. H., and Holt, E.: Two New Factors in Blood Coagulation—Heparin and Pro-antithrombin, Am. J. Physiol. **47:** 328, 1918.
5. Reed, C. I.: The Intravascular Use of Heparin, Am. J. Physiol. **74:** 79, 1925.
6. Howell, W. H.: Heparin: An Anticoagulant, Am. J. Physiol. **63:** 434P, 1923.
7. Howell, W. H.: The Purification of Heparin and Its Presence in Blood, Am. J. Physiol. **71:** 553, 1925.
8. Howell, W. H.: The Purification of Heparin and Its Chemical and Physiological Reactions, Bull. Johns Hopkins Hosp. **42:** 199, 1928.
9. Fuchs, H.: Blutgerinnung, Ergebn. d. Enzymforsch. **2:** 282, 1933.
10. Fonio, A.: Die Gerinnung des Blutes, Handb. d. norm. u. path. Physiol. Verlag, Julius Fischer, Berlin **6:** 307, 1928.
11. Morawitz, P.: Zur Frage der Blutgerinnung, Handb. der Biochemie. Verlag, Gustav Fischer, Jena **4:** 44, 1925.
12. Wöhlisch, E.: Die Physiologie und Pathologie der Blutgerinnung, Ergebn. d. Physiol. **28:** 443, 1929.
13. Zunz, E.: Traité de Physiol. (Roger et Binet) **7:** 189, 1934.
14. Howell, W. H.: Theories of Blood Coagulation, Physiol. Rev. **15:** 435, 1935.
15. Eagle, H.: Recent Advances in the Blood Coagulation Problem, Medicine **16:** 95, 1937.
16. Eagle, H.: Coagulation of Blood, Macleod's Physiology in Modern Medicine, Ed. 8, p. 252, St. Louis, 1938, The C. V. Mosby Company.
17. Nolf, P.: The Coagulation of the Blood, Medicine **17:** 381, 1938.
18. Fuchs, H. J.: Die Rolle des Prothrombins bei der Blutgerinnung, der Muskelaktion und der Infektionsabwehr, Ergebn. d. inn. Med. u. Kinderh. **38:** 173, 1930.
19. Fuchs, H., and Hartmann, E.: Ueber Proteolytische Fermente in Serum. X. Die Bedeutung des Komplements bei der Blutgerinnung. Ztschr. f. Immunitätsforsch. u. exper. Therap. **58:** 1, 1928.
20. Charles, A. F., and Scott, D. A.: Studies on Heparin. II. Heparin in Various Tissues, J. Biol. Chem. **102:** 431, 1933.
21. Holmgren, H., and Wilander, O.: Beitrag zur Kentniss der Chemie und Funktion der Ehrlichschen Mastzellen, Ztschr. f. mikr.-anat. Forsch. **42:** 242, 1937.
22. Jorpes, E., Holmgren, H., and Wilander, O.: Über das Vorkommen von Heparin in den Gefasswänden und in den Augen, Ztschr. f. mikr.-anat. Forsch. **42:** 279, 1937.
23. Jaques, L. B., Charles, A. F., and Best, C. H.: The Administration of Pure Heparin, Acta Med. Scandinav. (Suppl.) **90:** 190, 1938.

24. Chargaff, E., and Olson, K. B.: Studies on the Chemistry of Blood Coagulation. VI. Studies on the Action of Heparin and Other Anticoagulants: The Influence of Protamine on the Anticoagulant Effect In Vivo, J. Biol. Chem. **122:** 153, 1937.
25. Mellanby, J.: Heparin and Blood Coagulation, Proc. Royal Soc. London (Series B), **116:** 1, 1934.
26. Quick, A.: On the Action of Heparin and Its Relation to Thomboplastin, Am. J. Physiol. **123:** 712, 1938.
27. Quick, A.: Is Heparin an Antiprothrombin? Proc. Soc. Exper. Biol. & Med. **35:** 391, 1936.
28. Quick, A.: The Normal Antithrombin of the Blood and Its Relation to Heparin, Am. J. Physiol. **123:** 712, 1938.
29. Eagle, H.: Studies on Blood Coagulation. I. The Role of Prothrombin and of the Platelets in the Formation of Thrombin, J. Gen. Physiol. **18:** 531, 1935.
30. Eagle, H., and Harris, T. N.: Studies on Blood Coagulation. V. The Coagulation of Blood by Proteolytic Enzymes (Trypsin and Papain), J. Gen. Physiol. **20:** 543, 1936.
31. Clowes, G. H. A.: On the Mechanism of Blood Coagulation. Am. J. Physiol. **42:** 610, 1917.
32. Fischer, A., and Astrup, T.: Stöchiometrische Bindungsverhaltnisse Zwischen Heparin und Gerinnungstoff, Biochem. Ztschr. **278:** 326, 1935.
33. Fischer, A.: Gerinnungszeit und Konzentration der Gerinnungsstoffes, Biochem. Ztschr. **278:** 320, 1935.
34. Eagle, H.: Coagulation of the Blood; from Macleod's Physiology in Modern Medicine (Bard), Ed. 8, p. 252, et seq., St. Louis, 1938, The C. V. Mosby Company.
35. Eagle, H.: Recent Advances in the Blood Coagulation Problem, Medicine **16:** 95, 1937.
36. Schmitz, A., and Fischer, A.: Über die chemische Natur des Heparins. II. Die Reindarstellung des Heparins, Ztschr. Physiol. Chem. **216;** 264, 1933.
37. Fischer, A., and Schmitz, A.: Über die chemische Natur des Heparins. I. Die Quantitative Bestimmung des Heparins, Ztschr. Physiol. Chem. **210:** 129, 1932.
38. Bergström, S., Jorpes, E., and Wilander, O.: Studies on Pure Heparin, Skandinav. Arch. Physiol. **76:** 175, 1937.
39. Schmitz, A., and Fischer, A.: Über die chemische Natur des Heparins. III. Einige Untersuchungen zur Konstitution des Heparins, Ztschr. f. physiol. Chem. **216:** 274, 1933.
40. Charles, A. F., and Scott, D. A.: Studies on Heparin. I. The Preparation of Heparin, J. Biol. Chem. **102:** 425, 1933.
41. Scott, D. A., and Charles, A. F.: Studies on Heparin. III. The Purification of Heparin, J. Biol. Chem. **102:** 437, 1933.
42. Jorpes, E.: The Chemistry of Heparin, Biochem. J. **29:** 1816, 1935.
43. Charles, A. F., and Scott, D. A.: Studies on Heparin. IV. Observations on the Chemistry of Heparin, Biochem. J. **30:** 1927, 1936.
44. Schmitz, A.: Ist das Heparin eine Chondroitinpolyschwefelsäure? Ztschr. f. physiol. Chem. **236:** 1, 1935.
45. Jorpes, E.: On Heparin, Its Chemical Nature and Properties, Acta Med. Scandinav. **88:** 427, 1936.
46. Bergström, S.: Über Polysaccharidesterschwefelsäuren mit Heparinwirkung, Ztschr. f. physiol. Chem. **238:** 163, 1936.
47. Chargaff, E., Bancroft, F. W., and Stanley-Brown, M.: Studies on the Chemistry of Blood Coagulation. II. On the Inhibition of Blood Clotting by Substances of High Molecular Weight, J. Biol. Chem. **115:** 155, 1936.
48. Chargaff, E.: Studies on the Chemistry of Blood Coagulation. V. Synthetic Cerebroside Sulfuric Acids and Their Action on Blood Clotting, J. Biol. Chem. **121:** 187, 1937.
49. Herrmann, H.: Über die Hemmung der Blutgerinnung durch basische Körper und deren Beziehung zu organischen Gerinnungshemmend Säuren, Skandinav. Arch. Physiol. **76:** 125, 1937.
50. Wadsworth, A., Maltaner, F., and Maltaner, E.: The Anticoagulative Action of Organic Acids and of Heparin, and the Organic Base Diethylamine, Am. J. Physiol. **119:** 80, 1937.
51. Jorpes, E., and Bergström, S.: Der Aminozucker des Heparins, Ztschr. f. physiol. Chem. **244:** 253, 1936.

52. Jorpes, E., and Bergström, S.: Heparin: A Mucoitinpolysulfuric Acid, J. Biol. Chem. **118:** 447, 1937.
53. Harrow, B., and Sherwin, C. P.: A Textbook of Biochemistry, p. 103 et seq., Philadelphia, 1935, W. B. Saunders Company.
54. Jorpes, E.: Über das Heparin und seine Anwendung als Ersatzmittel für Oxalat und Zitrat in der Klinik, Acta Med. Scandinav. (Suppl.) **89:** 139, 1937.
55. Astrup, T., and Jensen, H. B.: Chemistry of Heparin, J. Biol. Chem. **124:** 309, 1938.
56. Astrup, T., and Jensen, H. B.: Purification of Heparin, Skandinav. Arch. Physiol. **79:** 290, 1938.
57. Lison, L.: La Signification histochimique de la Metachromasie, Compt. Rend. Soc. de Biol. **118:** 821, 1935.
58. Lison, L.: Études sur la Metachromasie Colorants metachromatiques et substances chromotropes, Arch. de biol. **46:** 599, 1936.
59. Jorpes, E.: Über die Wirkungsweise des Heparins, Skandinav. Arch. Physiol. **80:** 202, 1938.
60. Fischer, A.: Zum Mechanismus der Hemmung der Blutgerinnung, Biochem. Ztschr. **240:** 364, 1931.
61. Fischer, A.: Untersuchungen über Muskelkoaguline, Biochem. Ztschr. **240:** 357, 1931.
62. Fischer, A.: Antiprothrombin and Globuline, Biochem. Ztschr. **244:** 464, 1932.
63. Henriques, V., and Klausen, U.: Untersuchungen über den Serumalbumin- und Serumglobulingehalt des Serums, Biochem. Ztschr. **254:** 414, 1932.
64. Earle, I. P., and Howe, P. E.: Antiprothrombin and Globulins, Science **77:** 213, 1933.
65. Oelkers, H.: Zur Frage der Globulinbildung durch Heparin, Klin. Wchnschr. **12:** 191, 1933.
66. Von Mutzenbecher, P.: Naturwissensch. **21:** 331, 1933.
67. Hooker, S. B., and Boyd, W. C.: The Alleged Transformation of Serum Albumin into Serum Globulins, Science **76:** 517, 1932.
68. Schmitz, A., and Fischer, A.: Über die Wirkung von Heparin auf Serumalbumin, Biochem. Ztschr. **259:** 53, 1933.
69. Schmitz, A., and Kühl, L.: Fortgesetzte Untersuchungen über Heparin. Die Inaktivierung des Heparins in Blut, Ztschr. f. physiol. Chem. **234:** 212, 1935.
70. Fischer, A., and Schmitz, A.: Über die Wirkung von Heparin auf Serumalbumin, Biochem. Ztschr. **259:** 61, 1933.
71. Fischer, A.: Studies on Coagulation of the Blood, Japanese J. Exper. Med. **13:** 223, 1935.
72. Chargaff, E.: Studies on the Chemistry of Blood Coagulation. VII. Protamines and Blood Clotting, J. Biol. Chem. **125:** 671, 1938.
73. Chargaff, E.: The Protamine Salts of Phosphatides with Remarks on the Problem of Lipoproteins, J. Biol. Chem. **125:** 661, 1938.

Review of Recent Meetings

REPORT OF WESTERN SURGICAL ASSOCIATION, FORTY-EIGHTH ANNUAL MEETING, DEC. 2 AND 3, 1938, OMAHA, NEB.

J. M. McCaughan, M.D., St. Louis, Mo.

(From the Department of Surgery, St. Louis University School of Medicine)

I. **Cystography in the Study of Difficulties Following Prostatic Surgery, Theodore H. Sweetser,** Minneapolis, Minn.—Dr. Sweetser showed some excellent cystograms obtained by means of injecting air through a urethral catheter into the bladder. He emphasized that cystography was a valuable guide in the treatment of prostatic obstruction; also that it was of value in diagnosis in patients with various complaints after prostatectomy. He further advocated its use as a follow-up after secondary treatment of postprostatectomy sequelae.

Discussion.—**Verne Hunt,** Los Angeles, Calif., stressed the value of pre- and postoperative cystograms. He regards air as safe and simple but is loath to rely on it, preferring the opaque media as having more universal application. At any rate, he said the cystogram should be considered only one part of the examination. **W. J. Carson,** Milwaukee, Wis., prefers intravenous retention cystograms. Particularly, he likes to avoid the catheter in the presence of pyuria. The question of air embolism was raised by Dr. Carson. **T. H. Sweetser,** in closing, said he felt there was little danger of air embolism. In his experience radio-opaque solutions have not been as accurate as air.

II. **An Improved Incision for the Radical Operation for Carcinoma of the Breast, Neil J. Maclean,** Winnipeg, Canada.—Dr. Maclean discussed a new incision for radical operation for carcinoma of the breast. After discussing the importance of wide skin removal, he enumerated the difficulties of subsequent closure and showed illustrations of his technique which was essentially a T-incision with the vertical limb of the T directed laterally toward the axilla. The closure of the flaps, he said, now can be made without unsafe tension as is often the case with either the Halstead or other types of vertical incisions.

Discussion.—**T. Orr,** Kansas City, Kan., objects to any incision which places the scar across the axilla and said there was no one incision satisfactory for all breast cancers. **A. E. Benjamin,** Minneapolis, Minn., chooses the incision best suited to case. He questioned the resulting axillary scar in Dr. Maclean's incision. **J. F. Percy,** Los Angeles, Calif., believes Dr. Maclean's incision suitable for early cases but personally prefers to leave the wound open. He stated that "cosmetics had no place in the treatment of cancer." Dr. Maclean, in closing, stated he prefers the vertical incision in cases with involvement of the axilla. He has not seen as many instances of skin metastasis with this incision as with the vertical types.

III. **The Calibrated Skin Graft. A New Principle and a New Type of Graft, Earl C. Padgett,** Kansas City, Mo.—Dr. Padgett described a method of cutting

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skin in one sheet of absolutely uniform thickness from any area of the body in any pattern and of any thickness desired, practically eliminating the chance of either a failure of "take" or a partial failure of "take" and giving a good cosmetic appearance along with good protection. The device used by Dr. Padgett consisted of a large cylinder similar to a kymograph drum, which had a sharp knife with micrometer adjustment. The blade was made to move to-and-fro across the long axis of the face of the drum. At the start the skin was fixed to the drum with rubber cement and as it was sliced off the drum was rotated simultaneously, the skin adhering to it.

Discussion.—**J. B. Brown,** St. Louis, Mo., exhibited some slides illustrating various types of grafts and stages of healing. He discussed the confusion of the terminology of split grafts. **H. W. Trusler,** Indianapolis, Ind., presented slides showing the use of roll grafts, particularly emphasizing difficulties and failures with thick, split grafts in areas which still harbor infection and commenting on the importance of bacterial tests. Dr. Padgett referred to the economic advantages of his method in saving the patient time and expense.

IV. **Hypospadias, a Report on the Use of a Depilated Scrotal Flap, Harry P. Ritchie,** St. Paul, Minn.—Dr. Ritchie thought that the reason for the multiplicity of operations for hypospadias was the fact that the problem has been approached on a regional basis. The nature of the problem, he believed, was not dissimilar from many other situations in the body where loss of tissue required reconstruction by mobilization either of adjacent tissues or their transplant from more distant areas. He then described the advantages and disadvantages of a number of the operative procedures which have been used and urged as superior the operation utilizing flaps cut from the genitals. An illustrated case report showing the use of a tubed scrotal flap was presented.

Discussion.—**Gatewood,** Chicago, Ill., believes Ritchie's operation is sound but has seen many failures with various operations. He does not believe the growth of hair within these channels is as serious a complication as many have believed. **J. B. Brown,** St. Louis, Mo., feels that a method which makes more skin available is an advantage. He emphasized the importance of the first stage and the avoidance of injury to the corpora cavernosa. **E. C. Padgett** advocated the use of the Foley catheter as an aid in keeping the child dry. Dr. Ritchie agreed with Dr. Brown on the importance of proper release of the penile adhesions and described further the difficulties encountered in the case in question.

V. **Hemorrhagic Tendency in Jaundice, With Special Reference to Its Treatment With Vitamin K, Waltman Walters** and **Albert M. Snell** (by invitation), Rochester, Minn.—Dr. Snell outlined the present concept of the causes of bleeding in jaundiced patients or in persons with biliary fistula. This complication, he argued, was due to a deficiency of prothrombin, which in turn was the result of a lack of vitamin K. Failure of vitamin K absorption, he said, could be explained on the basis of the exclusion of bile from the intestine and the associated damage to the liver. He presented a series of operative cases showing the decrease in prothrombin and the effect of the administration of vitamin K and bile salts in establishing and maintaining a normal level of prothrombin preoperatively and postoperatively. He mentioned briefly the method of obtaining vitamin K either from extracts of rotted fish meal or alfalfa.

Discussion.—**R. W. McNealy,** Chicago, Ill., cited some work on 800 cases of jaundice observed at Northwestern University showing that postoperative bleeding could be controlled with bile salts and viosterol. He also discussed the importance of a lack of vitamin P. He suggested blood transfusion and intravenous glucose before operation if the bleeding time (Ivy) was prolonged. Dr. Snell found no

antihemorrhagic factor for chicks in pure fish oils. He had no experience with the Ivy bleeding time but did not think there had been any conclusive demonstration of the effect of vitamin P deficiency. He agreed with Dr. McNealy on the importance of proper preoperative preparation. **F. W. Bancroft,** New York, N. Y., recalled the work of Quick on prothrombin in 1925 when it was suggested that bleeding might be due to a protein deficiency. He also advocated the use of vitamin K.

VI. **Anesthesia, Anesthetic Agents, and Surgery, Erwin R. Schmidt,** Madison, Wis.—Dr. Schmidt said that the science of anesthesia, together with the art, has advanced tremendously in the last fifteen years, based on research and better knowledge of basic science, so that it is a distinct field in medicine. The best anesthesia which may be obtained in the various hospitals will depend, he believes, upon the different factors involved; namely, equipment, training of the anesthetist, and training of the surgeon. The latest developments in anesthesia were briefly described. The application of this newer knowledge, together with the introduction of an anesthetist into the surgeon's team and the role that the surgeon has to play for the fullest working-out of this new cooperative endeavor, was described.

Discussion.—**W. H. Cole,** St. Paul, Minn., considered Dr. Schmidt's emphasis of closer cooperation between surgeon and anesthetist as highly important. He discussed the value of oxygen therapy, the blood pressure level during anesthesia, and the proper choice of preanesthetic drugs. **Gatewood,** Chicago, Ill., discussed the importance to the surgeon of an understanding of the four planes of anesthesia and urged that surgeons aid in the development of facilities for training anesthetists. **T. H. Sweetser,** Minneapolis, Minn., questioned the use of ether anesthesia in elderly individuals. **J. F. Percy** opposed the indiscriminate use of barbiturates preoperatively and cited a fatal case in which the patient had been given ten or twelve different agents. He preferred ether in his own practice. Dr. Schmidt emphasized the need for judgment in the selection of the anesthetic agent to fit the particular patient's need. He recommended Gudel's monograph for the fundamentals of anesthesia.

VII. **Tumors of the Neck, William Boyd** (guest speaker), Toronto, Canada.—Dr. Boyd, introduced by N. J. Maclean, Toronto, Canada, discussed the diagnosis of tumors of the neck. He stressed the importance of approaching the diagnostic problem with orderly thinking. In respect to various classifications of tumors of the neck he mentioned two human traits common to most classifiers; namely, those who "split" and those who "lump." He then presented a systematic classification of tumors of the neck and described the pathogenesis, pathology, and differential diagnostic features of each. His presentation was augmented by many excellent photographs. Particularly good were several taken from Dr. Hertzler's monograph.

VIII. **The Diagnosis and Treatment of Ewing's Tumor, Henry W. Meyerding,** Rochester, Minn.—Dr. Meyerding reviewed the cases of Ewing's tumor encountered at the Mayo Clinic for a period of more than twenty-five years. He explained that this lesion was frequently confused with osteomyelitis by surgeon, roentgenologist, and even by the pathologist. The response to roentgen radiation was a diagnostic test of great value. Dr. Meyerding then dealt with the choice and results of treatment by irradiation, surgery, and a combination of the two.

Discussion.—**R. D. Schrock,** Omaha, Neb., presented a case in which both osteomyelitis and Ewing's tumor developed in the same extremity. **K. Speed,** Chicago, Ill., exhibited slides showing the distribution of Ewing's tumor, osteogenetic sarcoma, and benign giant cell tumor. He said that Ewing's tumor was rare in

the Chicago area. He then discussed the pathogenesis, pathology, differential diagnosis, and treatment. **W. Cole,** St. Paul, Minn., emphasized the rarity of the lesion and the danger of confusion with osteomyelitis. Dr. Meyerding exhibited slides of additional cases.

IX. **Nonparasitic Cysts of the Liver: A Report of Two Cases and an Analysis of the Literature, John M. McCaughan,** and **Louis J. Rassieur,** St. Louis, Mo.—Dr. McCaughan reported two cases of nonparasitic liver cyst. The several theories which attempt to account for the origin of these cysts were mentioned briefly. A review of the literature and an analysis of a large number of the reported cases was made. This latter was done to see if a correlation of symptoms, physical and pathologic findings would yield data of diagnostic value. Treatment and its relation to the end results were discussed.

Discussion.—Dr. Rassieur discussed the difficulties of differential diagnosis and the need to have the condition in mind. He also outlined the method of treatment. **F. F. Attix,** Lewistown, Mont., cited an unpublished case of his own and exhibited some excellent illustrations showing the operative technique employed. **R. Bartlett,** St. Louis, Mo., reported also two unpublished cases and felt that in one instance had the cholecystogram not been misinterpreted a correct diagnosis might have been made. Dr. McCaughan cited the recent experimental work of Bogetto in Italy on the experimental production of single and multiple cysts of the liver in rabbits by the transplantation of gall-bladder epithelium to the liver.

X. **Single Trauma as an Etiological Factor in Carcinoma, William E. Leighton,** St. Louis, Mo.—Dr. Leighton presented an abstract of cancer histories from the Barnard Free Skin and Cancer Hospital with antecedent single trauma. No case was complicated by medicolegal or compensation considerations. He dealt with the evidence for and against single trauma as an etiologic factor in carcinoma.

Discussion.—**H. Davis,** Omaha, Neb., said that absolute proof was very difficult to obtain. He cited that a comparative study of war records did not indicate a higher evidence of cancer than that common to the general population in the same age group. Dr. Leighton exhibited photographs of two patients who developed epitheliomas on the face after razor cuts while shaving.

XI. **Indications for Splenectomy in Children, George B. Packard, Denver, Colo.**—Dr. Packard reviewed case reports of twenty splenectomies in young children. His series included patients with familial hemolytic uterus, idiopathic purpura hemorrhagica, splenic anemia, and splenomegaly with gastric bleeding. He also commented on other anemias possibly related to splenic disease and on Gaucher's disease. Following this he considered the criteria of positive indications for splenectomy and the preoperative and operative treatment.

Discussion.—**A. Montgomery,** Chicago, Ill., remarked that Dr. Packard's paper was timely because splenectomy has been performed somewhat indiscriminately. Mention should be made of splenectomy for trauma and for tumors of the spleen. **George Curtis,** Columbus, Ohio, said he had made special blood studies and examination of the splenic pulp and bone marrow in fifty-two splenectomies in an attempt to correlate these factors with the clinical course but the results were not striking. **C. Johnston,** Detroit, Mich., referred to several cases of icterus neonatorum gravis in which the blood changes were investigated after operation. **E. Miller,** Chicago, Ill., made a suggestion for improving the operative technique. Essentially his procedure is to retract the stomach out of the way and secure the entire splenic pedicle with a tourniquet before beginning the ligation of the individual vessels.

XII. **Technical Notes on Pediatric Surgery: (1) Hypertrophic Pyloric Stenosis and (2) Congenital Indirect Inguinal Hernia, Stanley J. Seeger,** Milwaukee, Wis.—Dr. Seeger stated that he considered the Ramstedt operation the standard treatment for hypertropic pyloric stenosis. He discussed the prevention of wound disruption and stressed the importance of the high incision. The necessity for a proper appreciation of the anatomic arrangement in the pyloric area he regarded as essential if one were to avoid failure to relieve the obstruction. Puncture of the duodenum at operation, he said, was not serious unless it went unrecognized and unrepaired. He then showed illustrations of the proper technique. Dr. Seeger spoke of the technical steps in dealing with the processus vaginalis in congenital inguinal hernia and stressed basic anatomic considerations.

Discussion.—**Albert Montgomery,** Chicago, Ill., agreed with Dr. Seeger on the superiority of the high incision but noted that he has seen wounds disrupt in spite of this. He described a method of palpating for these pyloric tumors. He tests for puncture wounds of the duodenal mucosa by pouring saline solution into the wound and looking for escaping gas bubbles. He prefers not to make traction on the cord and testis in hernia but to facilitate dissection by Bevan's technique of injection of water. **J. C. Masson,** Rochester, Minn., said that accurate closure of accidental perforations of duodenal mucosa should be done. In two cases he followed this with a gastroenterostomy. He also prefers general anesthesia. In these hernias he likes to wait until the child is walking (2 to 3 years of age). **Roland Hill,** St. Louis, Mo., stressed the importance of careful preoperative preparation. He prefers the Ramstedt operation and cited a case dying of pneumonia months after operation. Microscopically the tissue had healed perfectly. He feels that the hernia should be taken care of, surgically at least, by the age of 5 years. **Potts,** Chicago, Ill., discussed methods of preoperative management and cautioned against the excessive palpation of the pyloric tumor. **W. H. Cole,** St. Paul, Minn., discussed the feeding and other factors in postoperative management. **R. S. Sanders,** Memphis, Tenn., has modified the customary incision. He makes a vertical incision in the skin and rectus fascia and displaces the muscle laterally. He then divides the transversalis and peritoneum transversely. **W. Bartlett,** St. Louis, Mo., said that he had used this same incision with good results. Dr. Seeger described methods of wound closure to avoid disruption. He stated that he had assisted in ten gastroenterostomies in infants. There was one death, but results in the others were satisfactory.

XIII. **The Influence of Sutures on Operative Wounds, Clifford U. Collins,** and **J. E. Bellas** (by invitation), Peoria, Ill.—Dr. Bellas reported results of his researches on a new nonsuture material of nonanimal origin which he called plastigut. He demonstrated by means of photomicrographs the differences in tissue reaction with catgut silk and plastigut and explained that the first two, being foreign bodies of protein origin, always reacted more or less intensely, which in turn tended to hinder primary repair. He defined the characteristic of the hypothetical ideal suture and concluded from his experimental and clinical studies that in plastigut this ideal had been most nearly attained.

Discussion.—Dr. Collins compared the results with catgut, wire, and plastigut and found the last superior. The incidence of healing by first intention was increased and the patients could be out of bed at an earlier date. **E. Schmidt,** Madison, Wis., enumerated the criteria for the ideal suture material. He had used plastigut in experimental animals and humans with good results. **W. J. Thompson,** St. Louis, Mo., agreed in condemning the use of catgut and silk. He reviewed some personal experimental and clinical work with a new type of suture material obtained from animal membrane and exhibited slides to show satisfactory results. Dr. Bellas said that plastigut was a nonanimal substance derived from plastic

material similar to Dupont's lusite. In commenting on Dr. Thompson's work he questioned whether an absorbable material in the very nature of things could ever be entirely without reaction. He suggested that it might be very much delayed with Dr. Thompson's material. **H. K. Bonn,** Los Angeles, Calif., exhibited specimens of tubulized chromic catgut which he thought ideal for suturing a divided ureter or common duct.

XIV. **A Simple, Efficient Method to Diminish the Incidence of Primary and Secondary Infection in Surgical Wounds, Reginald H. Jackson** and **Reginald H. Jackson, Jr.** (by invitation), Madison, Wis.—Dr. Jackson, Sr., reviewed the methods of Hart and others to diminish air-borne infections in surgical wounds by sterilizing the air and considered other factors involved in primary wound healing. He proposed a simple method which in his experience has given satisfactory results. The method of Jackson was based on observation of frequent primary healing after soap and water cleansing of accidental wounds known to be contaminated. He used a soap made of soy bean oil and corn oil, saponified with potassium salts. Had 200 consecutive cases without a single infection. He then exhibited moving pictures in color showing the technique.

Discussion—Dr. Jackson, Jr., described the technique used by them in taking their moving pictures. **O. H. Wangensteen,** Minneapolis, Minn., recalled Listerian times and then questioned the advisability of permitting large numbers of visitors to witness operations. He also discussed the problem of masks and adequate bacteriologic control of the operating room and its equipment. **H. W. Trusler,** Indianapolis, Ind., has utilized the same principle of cleansing tissue advocated by Dr. Jackson. He cited a case of a skin graft which failed, he thought, because of *Streptococcus hemolyticus* organisms probably hidden in the scar. **M. L. Mason,** Rochester, Minn., cited the rate of growth of various organisms in tissues as a reason for early mechanical cleansing with soap and water. Dr. Jackson, Sr., emphasized again that there was no particular bactericidal virtue in the soap itself, but that careful mechanical cleansing was essential for best results.

XV. **Experiences With Employment of Suction in the Treatment of Acute Intestinal Obstruction: A Reiteration of the Indications, Contraindications, and Limitations of the Method, Owen H. Wangensteen,** Minneapolis, Minn.—Dr. Wangensteen reviewed his experiences since 1931 in the treatment of acute intestinal obstruction by means of suction applied to an indwelling duodenal tube. This included consideration of the indications, contraindications, and the limitations of the method and the importance of correlating well all clinical and roentgen data. He emphasized most particularly the importance of accurate differential diagnosis. An effort, he said, should be made to answer the following questions before blindly instituting treatment: (1) Is there intestinal obstruction? (2) Is strangulation present? (3) Is the obstruction in the small or large intestine? (4) Is the obstruction complete or incomplete? He then presented statistics showing the comparative results in 156 cases of acute mechanical obstruction. There were 57 cases in which suction alone was employed. The mortality in the entire group was approximately 18 per cent. The mortality in the cases decompressed satisfactorily by suction was 7 per cent.

Discussion.—**E. Schmidt,** Madison, Wis., discussed the underlying physiology and biochemistry in relation to intestinal obstruction. He sought for an explanation of such symptoms as colic and slow pulse. He advocated the method of treatment outlined by Dr. Wangensteen and concluded with a plea for earlier diagnosis. **T. G. Orr,** Kansas City, Kan., considered Dr. Wangensteen's work the greatest contribution to the subject next to operation and urged use of the suction treatment but cautioned against overlooking cases of strangulation because of

temporary improvement. He did not believe alleged local irritation of the tube of more than minor importance. **A. Montgomery**, Chicago, Ill., questioned erosion of the esophageal and gastric mucosa from irritation of the tube. **Charles Johnston,** Detroit, Mich., commended Dr. Wangensteen's contribution and emphasized the importance of introducing the tube past the pyloric ring, which in his hands was not always easy to accomplish. He cited eighty-seven cases of his own treated in this manner. Dr. Wangensteen described in detail his technique of introducing the tube and securing duodenal intubation. He answered Dr. Montgomery by citing a case which came to post mortem after fifty-six days of drainage. No erosions of the gastrointestinal mucosa were noted.

XVI. **Peptic Ulcer, Intractable or Recurrent, F. Gregory Connell,** Oshkosh, Wis.—Dr. Connell's paper dealt with the surgical management of intractable or recurrent peptic ulcers. He considered the etiologic and pathogenic factors and the complications to which these ulcers are subject. The pathologic physiology of hyperacidity was discussed and the necessity of diminishing the acid secretion rather than attempting solely to increase the neutralization factors was emphasized. Therefore, he advocated a combination of nonoperative (diet and antisecretagogues) and operative (vagus resection and partial fundusectomy) measures.

Discussion.—**C. S. Williamson,** Green Bay, Wis., commented on the failures of operative and medical treatment. He said that hyperacidity per se was probably not important unless the normal mechanism for neutralization was deficient and in support of this view cited the experimental work of Mann and Williamson on duodenal drainage. **J. Berman,** Indianapolis, Ind., discussesd the relations of high gastric acid to ulcer and cited experimental work of the stimulation to mucin formation by Brunner's glands and the fact that low mucin values were found in patients with high stomach acids. He described a type of pyloroplasty which he favored. **R. R. Best,** Omaha, Neb., cited a recent case of intractable recurrent gastrojejunal ulcer in which he undertook an extensive resection.

XVII. **The Management of Megacolon, Claud F. Dixon** and **J. A. Bargen** (by invitation), Rochester, Minn.—Dr. Dixon said that while sympathectomy might be of value in the treatment of Hirschsprung's disease in children and in patients under 20 years of age, in older individuals resection of the colon was the procedure of choice. In four of his cases treatment consisted in a removal of the entire colon with the exception of the lower sigmoid and rectum, after which the ileum was anastomosed to the rectosigmoid. The operative technique was demonstrated in a colored moving picture. The results from this type of management, he declared, had been most encouraging.

Discussion.—**W. T. Peyton,** Minneapolis, Minn., defended sympathectomy for megacolon and stated that while there might not be anatomic return to normal yet function may be improved. The general mortality of exteriorization, he felt, was too high. He advocated further study of ganglion cells in these cases. Dr. Dixon agreed that good function may follow sympathectomy in selected cases but regarded appendicostomy as inferior to either sympathectomy or resection.

XVIII. **The Surgical Significance of the Motor Activity of the Human Stomach, George M. Curtis** and **Frank E. Hamilton** (by invitation), Columbus, Ohio.—Dr. Hamilton reported studies on the motor activity of the human stomach, first under normal conditions and then the effects of unilateral and bilateral splanchnic resection, vagotomy, herniorrhaphy, and cholecystectomy. He reported that biliary diseases increased the activity of the stomach, while immediately following a laparotomy gastric motility was decreased up to three days; subsequently, a

hypermotility ensued. This increased activity was associated with the occurrence of "gas pains." The effects of morphine, atropine, ephedrine, and prostigmin upon the disturbed postoperative motility were investigated.

Discussion.—**T. Orr,** Kansas City, Kan., discussed the clinical applications of Dr. Hamilton's researches and cited his personal interest in the action of morphine and prostigmin on the stomach and intestines. **Gatewood** mentioned similar experiments in which he engaged several years ago. The results were somewhat different. He thought that the same patient might give variable results at different times. Dr. Hamilton answered Dr. Gatewood on the variability of results in the same patient by citing a case of vagotomy which gave identical results after an interval of two years.

XIX. **Glimpses Into the History of Surgery** (Presidential Address), **Casper F. Hegner,** Denver, Colo.

XX. **The Treatment of Penetrating Wounds of the Lung, John M. Foster, Jr.,** Denver, Colo.—Dr. Foster called attention to the fact that the real mortality following lung penetrations occurred within a few minutes to a few hours following the accident as a result solely from a sudden, massive hemothorax and that any expectant means of treatment was obviously doomed to failure. The treatment of choice in his experience was early aspiration of the pleural blood with replacement by air. The advantages and technique of the collapse therapy were discussed in detail and illustrated with case reports.

Discussion.—**W. D. Gatch,** Indianapolis, Ind., emphasized the value of autotransfusion and in desperate cases made the suggestion that the aspirated blood be citrated and part set aside for later use. **G. E. Cheley** thinks mortality still is too high, urges earlier diagnosis of exact nature of injury. He preferred surgery in the severer forms with large vessel injury at the hilus of the lung. **J. D. Bisgard,** Omaha, Neb., asked about air embolism. **O. H. Wangensteen,** Minneapolis, Minn., suggested that the coexistence of an unsuspected bronchial fistula might be the cause of the "irreducible minimum" in mortality figures. He urged early recognition of this complication. **R. T. Vaughn,** Chicago, Ill., likewise asked about the danger of air embolism. **C. F. Hegner,** Denver, Colo., described in detail the technique of the procedure. He felt that the compression would close a bronchial fistula. He stressed the point that the simplicity of the technique and apparatus needed made the method available anywhere and to anyone; whereas, the radical operation called for a high degree of experience and skill. Dr. Foster thought the idea of citrating part of the aspirated blood a good one. He said he had never seen air embolus follow the injection. He also described the technique of injection in detail.

XXI. **Compound Fractures Around the Elbow Joint, Illustrated With Lantern Slides, William R. Cubbins,** Chicago, Ill.—This paper discussed the treatment of compound wounds from an operative standpoint, from a prophylactic standpoint, with tetanus and gas antitoxin, and submitted a new method for extension, which essentially was the insertion of an ordinary screw type of hook into the ulna. He also described in detail the technique of suturing the olecranon to the triceps muscle. In dealing with compound fractures he urged thorough mechanical cleansing and complete débridement of the wound which was then to be closed loosely. Dressings, he said, should be of dry sterile gauze and should be changed every six hours to promote capillary drainage. Accurate immediate approximation of the bone fragments he considered secondary in importance to thorough cleansing of the wound. He preferred to give gas bacillus and tetanus antitoxin in massive doses rather than in the customary prophylactic amounts. He then outlined his method of treatment for active gas bacillus infections.

Discussion.—**F. D. Dickson,** Kansas City, Mo., stressed the importance of early recognition and immediate treatment. His experience with ordinary prophylactic doses of serum in these cases of potential gas bacillus infection has been satisfactory. **J. Jackson,** Madison, Wis., discussed injury to the brachial artery in anterior and posterior elbow joint dislocations and cited a personal case in which he successfully anastomosed a severed brachial artery. **E. L. Gilcreest,** San Francisco, Calif., commented on the importance of elevation of the elbow joint and proper position of the forearm, and also on the value of beginning early motion in fingers and toes. **L. F. Barney,** Kansas City, Kan., asked about débridement after a twenty-four-hour lapse. Dr. Cubbins said it was his practice to remove all dead or dying tissue when found.

XXII. **Repair of Eversion of Vagina, With or Without Pelvic Viscera, Lester D. Powell,** Des Moines, Ia.—Dr. Powell described an operation which utilizes the rectus fascia for the support of the vaginal vault or pelvic structures. His operation essentially is to dissect out a triangular flap from the rectus fascia. This flap is bisected and next the two halves are carried into the pelvis where they are attached either to the uterus, the cervical stump, or the tissues of the vaginal vault, as the case might be.

Discussion.—**O. J. Fay,** Des Moines, Ia., said that he had seen and examined both of Dr. Powell's cases. He had also used the operation on one patient with satisfactory results. **V. C. Hunt,** Los Angeles, Calif., thought Dr. Powell's operation possessed certain advantages over other procedures, particularly where the cervical stump could not be brought up for fixation. Dr. Powell said he would rather not have it referred to as the Powell operation until it had proved its worth.

XXIII. **Giant Cell Tumor of the Humerus, Percy D. Peabody,** Webster, S. D.—Dr. Peabody reported a case which became malignant after having been diagnosed as nonmalignant by experienced pathologists who studied the biopsy specimens and even the complete amputated specimen. Disarticulation of the shoulder was done and this was followed by rapid recurrence in the operative scar and early lung metastasis.

Discussion.—**Wallace Cole,** St. Paul, Minn., quoted Dr. Geschichter on the relative benign character of giant cell tumors but suggested that a small area of malignancy must have been overlooked. He urged closer correlation of the clinical, radiographic, and pathologic data. **M. Henderson,** Rochester, Minn., recalled his own impression of this case and enumerated some of the difficulties experienced in its study. **K. Speed,** Chicago, Ill., reported a case of his own in which a giant cell tumor was removed locally and five years later recurred with evidence of inguinal node involvement. Amputation was done but sections were not yet available. He thought either an osteogenetic sarcoma or a malignant degenerative process in the giant cell tumor likely.

REPORT OF THE ANNUAL MEETING OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA AT PITTSBURGH, PA., NOV. 28—DEC. 2, 1938

LEO G. RIGLER, M.D., MINNEAPOLIS, MINN.
(From the University of Minnesota)

AT THE annual meeting of the Radiological Society of North America many important papers on roentgen diagnosis and radiation therapy were presented. Only those of particular surgical interest will be reviewed here.

The value of the upright position in **Gall Bladder Examinations** was recapitulated by **Alice Ettinger,** Boston, Mass. She reviewed the work of Åkerlund and Bernstein and brought out the importance of this maneuver in the detection of small stones. In this manner is demonstrated the layering of bile in the gall bladder and the method by which concentration occurs. Cholesterin stones will float in iodine-containing bile, but not in normal bile. **George Levene, R. M. Lowman,** and **E. G. Wissing,** Boston, Mass., discussed the **Roentgen Diagnosis of Strawberry Gall Bladder,** pointing out that many cases of cholesterosis are diagnosed as normal by ordinary cholecystographic methods. They laid down certain criteria for the roentgen differentiation of the strawberry gall bladder from chronic cholecystitis, but failed to indicate convincingly how these findings differed from the normal.

The Roentgen Diagnosis of Union in Fractures of the Femoral Neck was discussed by **L. H. Garland,** San Francisco, Calif., who emphasized the difficulty of determining bony union in such cases. He believes that union cannot be predicted with certainty in less than twelve months after the injury, that weight-bearing must first be undertaken, and that bone trabeculae must be observed to extend across the fracture line before union can be established. Garland warned against appearances in the roentgenogram which simulate bony union.

A symposium on **Low Back and Sciatic Pain** was presented by a number of essayists. **M. N. Walsh,** of the Mayo Clinic, detailed the clinical and neurosurgical aspects of herniation of the intervertebral disk, emphasizing the frequency of this condition as a cause of low back pain. He presented data on 300 cases in which 332 herniations of the disk had been diagnosed. The use of clinical criteria, such as intractable low back pain or sciatica, the reversed Quackenstedt test, and the character of the spinal fluid, to select patients for myelography was detailed. **P. B. Steele,** Pittsburgh, Pa., emphasized the frequency of low back pain in the presence of normal roentgenograms, while **R. S. Bromer,** Philadelphia, Pa., demonstrated the numerous congenital anomalies and anatomic variations which might be observed roentgenologically, but whose clinical significance was not established. **W. E. Chamberlain** and **B. R. Young,** Philadelphia, Pa., reported on 150 cases of myelography, using O_2 as a contrast medium. They find it satisfactory in many cases both for the diagnosis of intervertebral disk herniation and for cord tumors. It has the advantage that it is free from deleterious effects or dangers and when serious doubt occurs the examination may be repeated using lipiodol. They emphasized the importance of posture in the demonstration of ruptured disks, both during roentgen examination and at operation. **J. D. Camp,** of the

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Mayo Clinic, reported roentgen examination by myelography in 253 cases of spinal cord lesions, including 205 cases of ruptured intervertebral disk, 5 cases of thickened ligamentum flavum, and 43 cases of spinal cord tumor. The accuracy of diagnosis using 5 c.c. of lipiodol is extremely high both as to localization and as to the nature of the lesion. He believes there is no real harm done by myelography with iodized oil and is doubtful whether myelography with O_2 is sufficiently accurate to justify its use. In the discussion Garland reported on 35 cases examined from one to twelve years after myelography with 5 c.c. of lipiodol, in none of which could be found any subjective or objective signs of cord or nerve injury due to the contrast substance.

E. J. Ryan, New York, N. Y., reported several cases of duodenal ulcer with the clinical syndrome of gall-bladder disease. He believes duodenal ulcer and cholecystitis are frequently associated, the gall-bladder disease being caused by the inflammatory process in the duodenum. **The Roentgenological Differential Diagnosis Between Diverticulitis and Cancer of the Colon** was presented by **R. Schatzki,** Boston, Mass. He pointed out that this differentiation must be made preoperatively largely on the roentgen findings as these conditions can seldom be distinguished at operation. The high mortality of resection in cases of diverticulitis makes it vital to determine which condition is present. He detailed the differential roentgen signs, emphasizing the importance of detailed examination of the local area with compression and "spot film" technique. The use of air is somewhat dangerous. In cases of obstruction in which the area of the lesion could not be filled with barium, he advocates preliminary cecostomy for relief of obstruction followed by re-examination roentgenologically within a week or two when the obstruction will usually have been relieved and visualization of the involved area can be obtained.

George White, Boston, Mass., described a method of impregnating soft rubber drains, such as the Penrose or cigarette drain, with barium sulfate, thus making it opaque to roentgen rays. It is possible to determine the presence and location of such a drain in an empyema cavity even if it is filled with fluid. The various properties of such a rubber drain are not impaired by such chemical preparation.

The papers on radiation therapy were presented largely in the form of symposiums. Carcinoma of the breast was discussed by a number of essayists. **H. B. Hunt, N. F. Hicken,** and **T. T. Harris,** Omaha, Neb., presented their work on roentgen diagnosis of breast diseases using contrast media. They advocate skiodan viscous (Winthrop) and CO_2 insufflation. **E. R. Whitmore,** Washington, D. C., detailed his observations on the dissemination and metastasis of carcinoma of the breast by the use of whole organ sections. These demonstrate vividly the extensive infiltration of the breast tissue with cancer cells, in inflammatory carcinoma, the permeation of the lymphatics of the breast and fascial plexus, and extension to the liver. **F. E. Adair,** New York, N. Y., advised the use of aspiration biopsies of the breast in cases with palpable axillary glands followed by preoperative irradiation using very heavy doses of x-radiation. Six weeks later operation is done. This method is not used in the aged, in cases of lung fibrosis, or marked anemia.

C. F. Geschickter, Baltimore, Md., related his experiences with the use of subcutaneous pellets of estrin implanted in mice. By implanting in this manner long-continued, slow absorption occurred and with relatively small doses he produced mammary cancer. The statistical analysis indicates a definite correlation between the estrin and the development of the tumors. He also pointed out the necessity for examination of urine throughout the entire menstrual cycle if proper assays of prolan are to be obtained.

A paper on **Recovery Following Human Ovarian Irradiation** was presented by **H. W. Jacox,** Pittsburgh, Pa., who reported a patient surviving five years after removal of a huge malignant ovarian tumor. In spite of extensive postoperative roentgen therapy followed by artificial menopause for three years, she later went through a normal pregnancy and puerperium and had a normal baby.

J. R. Carty and **B. S. Ray,** New York, N. Y., demonstrated a method of low voltage roentgen therapy of neurological tumors, directly applied with a mobile apparatus in the operating room, after exposure of the tumor. Some favorable effects have been observed. **J. F. Kelly,** Omaha, Neb., also presented the results of treatment with a mobile apparatus at the bedside particularly in cases of acute peritonitis, gas gangrene, surgical parotitis, pneumonia, acute osteomyelitis following compound fractures, post-partum infection, Ludwig's angina, erysipelas, and other infections. **M. W. Berck** and **W. Harris,** New York, N. Y., reviewed again their experiences with the roentgen treatment of bronchiectasis. In 80 cases, 50 per cent have had practically complete cessation of cough, foul expectoration, and toxemia. These patients achieve a social and economic rehabilitation and exhibit a "dry" bronchiectasis as the end-result.

A symposium on the differences between 200 kv. and supervoltage roentgen therapy brought out the conflicting opinions of a number of investigators. **H. Schmitz,** Chicago, Ill., reported on five-year end-results in carcinoma of the uterus and breast and believes his results are distinctly better using 800 kv. as compared to 300 kv. x-rays previously used. Likewise **Richard Dresser, J. C. Rude,** and **B. J. Cosman,** Boston, Mass., believe their results, especially in bladder tumors, were greatly improved by using 1,000 kv. x-rays. **W. E. Costolow,** Los Angeles, Calif., reviewed the five-year end-results using 500 kv. x-ray therapy especially in advanced cases of carcinoma of the cervix. He also believes the results are moderately improved over those obtained with lower voltages. In the discussion by various radiologists the numerous factors of error inherent in such comparisons were brought out. The opinion was general that no marked superiority of supervoltage radiation therapy had yet been clearly established.

THE THIRD INTERNATIONAL GOITER CONFERENCE, WASHINGTON, D. C., SEPT. 12-14, 1938

F. T. H'Doubler, Ph.D., M.D., Springfield, Mo.

THE Third International Goiter Conference was held in Washington, D. C., Sept. 12, 13, and 14, 1938. The two previous conferences were held in Berne, Switzerland, in 1927 and 1931. Undoubtedly the uncertain political situation in Europe, which was at a high pitch at the time of the Conference, was responsible for keeping away a number of participants. As it was, in addition to those from the United States, there were speakers from Switzerland, Cuba, Mexico, Argentina, Colombia, Poland, Roumania, France, Germany, and Italy, with Switzerland leading the foreign countries in the number of different speakers. All of the papers, except two, were read in English.

The American Association for the Study of Goiter caused its fifteenth annual meeting to occur at the same time and place as that of the Third International Goiter Conference and was host to the Conference. The meetings and programs of the two bodies were merged. There are no official connections between the Conference and the American Association as to membership; that is to say, membership in the one organization does not automatically require or furnish membership in the other.

Headquarters for the joint meeting were at the Mayflower Hotel, where on Monday morning, Sept. 12, the Conference was called to order by **H. H. Kerr,** Washington, D. C., chairman of the committee in charge of local arrangements. Very suitable greetings from the **Honorable Cordell Hull,** Secretary of State, were followed by a short address by **Frank Lahey,** Boston, Mass., President of the American Association for the Study of Goiter. Dr. Lahey gave his address in turn in English, German, French, and Italian.

The Conference proceeded to organization and election of officers. **Frank Lahey** was elected president and **W. Blair Mosser,** Kane, Pa. (secretary of the American Association for the Study of Goiter), was elected secretary. The following honorary presidents were elected: **Theodore Lang,** Münich, Germany; **Henri Welti,** Paris, France; **H. Eggenberger,** Herisau, Switzerland; **S. Tubiazz,** Warsaw, Poland; **C. Wegelin,** Berne, Switzerland; and **Pedri Cossi,** Buenos Aires, Argentina.

The organization then took up its scientific program. Fifty-five papers were listed for delivery over a three-day period. Obviously it would be very unsuitable in reporting this meeting to abstract each paper, and to abstract some and not others not only would amount to slights but also would impose upon the reader the reporter's bias of interest and importance. Consequently only the general trends of the meeting will be reported. Transactions of the meeting, including all the contributions read and those by title, can be had by communicating with **Frederick A. Coller,** Chairman, Ann Arbor, Mich.

The first portion of the beginning morning's program was given over to the subjects of endemic goiter, cretinism, and childhood myxedema. The direct relation of the incidence of endemic goiter and cretinism to the amount of geographical radioactive emanation and the inverse relation to geographical thorium emanation were brought out. A sharp distinction was made between childhood myxedema and

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cretinism. It was emphasized that geographical location is more important than any other factor (source of water, etc.) in relation to endemic goiter and cretinism. The second portion of the morning's program dealt with iodine metabolism (blood iodine levels, hormone iodine, urinary and fecal elimination of iodine) in relation to normal and abnormal thyroid function.

In the afternoon of the first day there was a variation of subjects ranging through studies of thyroid secretion, the effects of thyroid extract, thyroiditis, Riedel's struma, Hashimoto's struma, and malignant goiter. One of the high points of the meeting was the groups of papers on thyroiditis and malignancy of the thyroid and their discussions. The papers on malignant thyroid brought out that papillary tumors of the thyroid stand in one class regardless of origin and that with them prognosis is best, and that next in line in this respect is the malignant adenoma; whereas the prognosis is worse with the diffuse type with polymorph infiltration, and with the lymphosarcoma. The degree of malignancy of a thyroid tumor might be said to be proportional to its departure from the papillary form. Such factors as the patient's age and general condition, sensitivity of tumor to radiotherapy, histology pattern, etc., were discussed as was also the relation of time of discovery of malignancy (before, during, or after operation) to prognosis.

In the evening a very convincing group of papers was read on goiter prophylaxis, showing the efficacy of iodine both in Europe and in widely separated places in America.

The morning's program of the second day dealt with endocrinology in general (the combinations of disturbances of fourteen hormones can create 15,000,000 different changes!), the pituitary in relation to metabolism (describing a pituitary hormone that depresses carbohydrate metabolism, probably decreases protein metabolism, and greatly increases fat metabolism), the relation of pituitary to thyroid disease, the relation between vitamin A deficiency and thyroid disease, embryologic considerations relating to the thyroid, and sterol deposition after thyroidectomy. In the afternoon there was a wide variation of subjects including several on carbohydrate metabolism and several on the pituitary thyrotropic hormone. **George W. Crile,** Cleveland, Ohio, read a very fine paper on the **Mechanism of Hyperthyroidism.**

At the annual business meeting of the American Association for the Study of Goiter, **J. K. McGregor,** Hamilton, Ontario, was elected president; **Claud Hunt,** Kansas City, Mo., vice-president. **W. B. Mosser,** Kane, Pa., **George C. Shivers,** Colorado Springs, Colo., and **V. E. Chesky,** Halstead, Kan., were re-elected corresponding secretary, recording secretary, and treasurer, respectively.

The official banquet of the Conference was held in the evening.

On the final day in the morning session papers were given on experimental studies of exophthalmos and on the pathology of thyroid activity; also papers on various phases of thyroid disorders (anxiety overstimulation, toxic adenoma, hyperthyroidism with low basal metabolic rate, goiter heart, and recurrent hyperthyroidism) and a paper on iodine thyrotoxicosis. In the final afternoon the papers dealt with the medical treatment of hyperthyroidism, the use of vitamin B_1 in preoperative preparation, x-ray therapy, recurrent thyrotoxicosis, fallacy of iodine therapy after bilateral thyroidectomy, and hyperthyroidism in children; the discussion of the latter was accompanied by interesting x-ray films showing advanced skeletal development, the opposite of that found in cretinism or childhood myxedema. **Frank Lahey,** the president of the Conference and of the American Association for the Study of Goiter, read an excellent paper on **Surgery in Hyperthyroidism,** pointing out that in borderline cases firmness of the gland tends to point to toxicity. He advocated adequate exposure (furnished by cutting the muscles), a dry field, good light, and magnification, in identifying and thereby avoiding removal of or injury to

the parathyroids. Tissue removed should be inspected for parathyroids and any found should be transplanted. He also advocated demonstration of the recurrent laryngeal nerve to protect it against injury.

Allen Graham, Cleveland, Ohio, and his committee deserve much credit for their fine work in arranging so splendid a program.

ANESTHETISTS' TRAVEL CLUB MEETING, OCT. 10-15, 1938

EDWARD B. TUOHY, M.D., M.S.(ANES.), ROCHESTER, MINN.
(From the Section on Anesthesia, the Mayo Clinic)

THE meeting of the Anesthetists' Travel Club was held at Madison, Wis., on Oct. 10 and 11; at Rochester, Minn., on Oct. 12 and 13; and at Minneapolis, Minn., on Oct. 14 and 15. The clinical demonstrations and seminars in anesthesia at Madison were conducted at the Wisconsin General Hospital by **R. M. Waters** and his associates. Inhalation anesthesia was demonstrated for a variety of surgical cases, using predominantly cyclopropane. The intratracheal method of general anesthesia with cyclopropane as the anesthetic agent was used frequently. The technique of controlled respiration for patients anesthetized with cyclopropane was demonstrated by various members of the department. The seminars in anesthesia and related subjects conducted at the Wisconsin General Hospital were given by various members of the university staff, including **W. J. Meek,** professor of physiology, who presented a paper on vasoconstrictors. He and his associates have been studying epinephrine, cobefrin, synephrin, neosynephrin, arterenol, paredrine, and many other sympathicomimetic drugs and it is their opinion that the toxicity of neosynephrin on the heart determined by electrocardiographic studies on dogs is the least of any of the vasoconstrictors studied.

An interesting discussion of the relationship of vitamins to anesthesia and of the transportation of oxygen and carbon dioxide in the blood was presented by several members of the Department of Agricultural Physiology. The importance of vitamin B in relation to the yellow respiratory enzyme of Warburg was discussed also.

In Rochester the Travel Club attended the clinical and experimental demonstration on anesthesia and related subjects held at the Mayo Clinic. The use of local and regional, intravenous, and inhalation anesthesia was demonstrated at the various hospitals by members of the Section on Anesthesia. The research work that is being carried on in anesthesia was demonstrated at the Institute of Experimental Medicine. **T. H. Seldon** demonstrated the activity of the capillaries in the ears of normal and anesthetized rabbits. **L. H. Mousel** presented a new device for the administration of inhalation anesthetic agents to small animals. **E. J. Baldes, J. F. Herrick,** and **H. E. Essex** demonstrated a new electrical method of measuring blood flow and blood pressure in animals.

A symposium on anesthesia was presented at the general meeting of the staff of the Mayo Clinic, which included a presentation by **E. J. Delmonico** on **Tests for Derivatives of Barbituric Acid,** one by **L. H. Mousel** on **Effect of Some Respiratory Stimulants on Experimental Animals Anesthetized With Pentothal Sodium** and one by **J. S. Lundy** on **A Closed Method of Venipuncture and a Hand Roller for the Speedy Administration of Blood or Solutions for Intravenous Therapy.** Another seminar and discussion in anesthesia and related subjects in-

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cluded a presentation by **C. J. Betlach** on **Effect of Various Anesthetics on the Electrocardiogram;** by **P. W. Searles** on **Effect of Certain Anesthetics on the Blood** and by **D. V. Shepard** on **Blood Transfusion.** Discussions were given by **E. J. Kepler** on **Diabetes as an Anesthetic Risk** and by **C. K. Maytum** on **Helium and Oxygen Treatment of Intractable Asthma. L. H. Mousel** gave a presentation on **Gas Analysis by the Effusion Method. W. M. Boothby** and **W. R. Lovelace** demonstrated **A New Type of Inhalation Apparatus for the Administration of Oxygen or Oxygen and Helium.**

Members of the Anesthetists' Travel Club spent Oct. 14 and 15 as guests of **Ralph Knight** and his associates at the University of Minnesota. Members of the Department of Physiology under the direction of **A. D. Hirshfelder** and **R. N. Bieter** and their associates demonstrated the injection of pressor drugs in spinal anesthesia in rabbits. The results of their experiments indicated that pitressin combined with other pressor drugs, such as epinephrine, ephedrine, neosynephrin, and others, gave better results in the maintenance of blood pressure than did any of these other pressor drugs used alone. In the Department of Physiology, **M. B. Visscher** and his associates presented studies of dynamics of the heart during anesthesia by means of the Starling heart-lung preparation from a dog. The method of preparation of the heart-lung experiment was demonstrated to the group. Dr. Visscher is carrying on studies on the effect of many anesthetic drugs on cardiac output. Dr. Visscher showed that the output of the heart was diminished by about 30 per cent when sodium amytal was administered to the heart-lung preparation. The decrease in cardiac output was accompanied by a fall in mean blood pressure and a decrease in coronary circulation. **R. T. Knight** presented a clinical demonstration which included the technique of peridural anesthesia and various methods of regional and general anesthesia.

J. R. Paine of the Department of Surgery of the University of Minnesota gave a demonstration for measuring the elasticity of the human lung. This is computed on the basis of the amount of force producing distortion in the pleural cavity in relation to the amount of "distortion produced by that force." Pneumothorax is performed and by means of a water manometer variations in pressure are determined. The pneumothorax needle is connected by means of a rubber tube to a chamber in which there are two mirrors, a tidal air mirror and an intrapulmonary pressure mirror, and the patient breathes through an apparatus consisting of a large number of small brass tubes. The mirror is attached on a tambour and is deflected by the flow of air. The light from this mirror registers on a moving photographic film. The developed film shows a continuous line alternately above and below a base line and from this the elasticity of the lung is measured. The definite clinical value of such an estimation has not yet been established.

After attending the clinics on anesthesia and surgery at the University Hospital, members of the Travel Club were taken through the manufacturing plant of the Heidbrink Company and were shown various anesthesia apparatus.

Book Reviews

The 1938 Year Book of General Surgery. Edited by Evarts A. Graham, Washington University, St. Louis, Mo. Cloth. Pp. 781, with 312 illustrations. Chicago, 1938, The Year Book Publishers. $3.

The idea of a year book in which the most important contributions to surgical literature are reviewed and the most significant advances discussed is a good one. A book of this sort, abstracting its articles almost solely from surgical literature, has of necessity a very definite practical objective in mind. Surgery, however, draws upon a wider range of knowledge than that concerned with diagnosis, recognition of the nature of pathologic conditions of surgical interest, and surgical technique. The reviewing of important articles in the interphase interests between surgery, bacteriology, biochemistry, and physiology would enhance the value of this work without detracting from its essential practical nature.

The Year Book Publishers are fortunate in having a man of the breadth and depth of view of Dr. Graham as its editor. That the editor knows his year book is apparent to anyone who thumbs through the pages of this volume. His acquaintance with the materials of previous year books is astounding, an observation which suggests that the editor enjoys the arduous tasks involved in the difficult labors of digesting literally thousands of articles. Very pertinent comments are made by him upon a large number of the abstracted reviews throughout the volume.

The entire range of surgery, except for the special provinces of the urologist, gynecologist and eye, ear and nose specialists, are reviewed. It would be difficult to mention, let alone select, the most significant contributions reviewed. The editor's introduction affords, in a way, a suggestion as to what he considers some of the more important material digested in the *1938 Year Book*. The writer of this review would commend especially the sections on anesthesia, asepsis, operative technique, and wound healing as containing much fundamental information for the enlightenment of all surgeons.

The Year Book is a handy reference manual to the surgical literature of the year and a valuable book for every surgeon to have within ready reach.

Meningiomas. Their Classification, Regional Behaviour, Life History, and Surgical End Results. By Harvey Cushing, M.D., with the collaboration of Louise Eisenhardt, M.D. Pp. 785, with 685 illustrations. Springfield, Ill., and Baltimore, Md., 1938, Charles C. Thomas, Publisher. $15.

Dr. Harvey Cushing, in collaboration with Dr. Louise Eisenhardt, presents a book on the meningiomas which is a fitting successor to the senior author's classic series of articles and monographs on tumors of the brain and spinal cord. The meningiomas are perhaps the most fascinating and difficult type of tumor which confronts the neurosurgeon. They make up only about 13 per cent of cerebral neoplasms, but are more frequently encountered than any single type of glioma. Nearly always a curable condition, provided they can be completely enucleated, they constitute a most stimulating challenge to the skill of the operator because of their all too common tendency to grow in inaccessible places, their vascularity, and the knowledge that they are liable to recur sooner or later unless their attachment to the dura and skull is thoroughly destroyed.

Three hundred and thirteen case histories with a follow-up period of from five to twenty-seven years form the background on which this book is built. Of these meningiomas, 18 originated in the spinal canal, the remainder within the skull. Only 2 of this long series of patients have been lost sight of. This gives an unparalleled opportunity to study the life history of this important group of tumors and to draw conclusions as to the most suitable method of surgical attack. It is also fascinating to trace the evolution of Dr. Cushing's technique. The operative mortality in the series of intracranial meningiomas operated upon in Baltimore prior to 1912 was 25 per cent. Through steady improvement this fell to a minimum of 8.3 per cent during his final five years at the Brigham Hospital. This dramatic change coincides with the increased use of blood transfusion, the reduction of excessive intracranial pressure by ventricular tap, saline irrigation of the wound and suction, also with such technical improvements as the silver clip and electrosurgical devices developed in Dr. Cushing's clinic.

Twenty-eight chapters of the book are devoted to a discussion of meningiomas in different areas. These are taken up in order of their geographical location, beginning with the rare instances without dural attachment and the infrequent tumors in the posterior fossa. This regional classification is continued up the base of the skull into the middle and anterior fossae, and then along the falx and out into the cranial convexity. Chapter 31 is devoted to the extraordinary case histories of two patients with recurring paracentral meningiomas on whom Dr. Cushing was forced to operate eleven and seventeen times respectively for rapid recurrences of the growth.

The four other chapters deal with historical aspects of the subject, a pathologic discussion of the meningiomas, a résumé of the intraspinal tumors, and an account of surgical technique and end results. It is of interest to note that one of the earliest cases in the series is alive and well 27 years after operation. Twelve other patients survived for over 20 years and an additional 67 for over 10 years. All together 132 patients are alive at the time of publication, 5 years after the last of the series was operated upon.

In conclusion the reviewer wishes to state that this work has given him greater pleasure than any other which it has been his privilege to review. It contains a wealth of material of great scientific value and references to over five hundred articles in the literature. The book is to be commended not only for the exceptional interest of its subject matter, but also for its readability and the uniform excellence of its 685 illustrations, which accompany nearly every page of the text.

Les Embolies Arterielles Des Membres. By H. Haimovici. Paper. Pp. 333, Paris, 1937, Masson et Cie. 55 francs.

In this monograph the author presents an extensive review of the European literature dealing with the problem of embolism of peripheral arteries, but his major conclusions are largely those of his teachers, R. Leriche and J. Fiolle. The material is presented in the form of a thesis. The author stresses the value of the collateral vessels and he describes clearly the mechanism and conditions under which an active collateral circulation establishes itself. The surgical methods of embolectomy and arteriectomy are presented as the most important therapeutic measures, but no mention is made of the frequency of secondary intravascular clotting of the blood at the site of the surgical operation on the artery. The author likewise has failed to take into consideration the important contributions concerning the effect of heparin upon the intravascular clotting of blood. The general care of the affected extremity and other conservative methods of treatment are entirely omitted. On the whole, the material is presented rather dogmatically and the author

does not seem to realize that there is still much to be desired from all the present modes of treatment of these serious clinical problems. The monograph should prove valuable to those who are especially interested in peripheral vascular disturbances since it does contain a good summary of the important clinical, pathologic, and therapeutic aspects of major and minor arterial accidents.

The Vitamins and Their Clinical Applications. By W. Stepp Kuhnan, Director of the Municipal Institute for Balneology and Metabolism, Wiesbaden, and H. Schroeder. Translated by Herman A. H. Bouman. Cloth. Pp. 173. Milwaukee, 1938, Wisconsin Cuneo Press, Inc.

This little manual on vitamins summarizes well the available information upon this important field up until 1936. In an appendix is included a larger list of English and American bibliographic references relating to the textual matter prior to and subsequent to the appearance of this monograph by its German authors. The appendix also contains brief sketches of the apparent function of each vitamin, the possible results of deficiency, as well as the results of absence of the vitamins in the diet.

In each chapter the historical aspects relating to the development of knowledge concerning the vitamin under consideration are briefly traced; the chemistry and occurrence of the vitamin, its mechanism of action, dosage, and man's requirement of it are discussed fully.

There is no field of medicine in which a knowledge of the vitamins is unimportant. Every practitioner would do well to accquaint himself with the advances which are being made in this aspect of nutrition. This monograph should prove a useful guide for the accomplishment of that purpose.

Industrial Surgery. Principles, Problems, and Practice. By Willis W. Lasher. Pp. 452, with 193 illustrations. New York, 1938, Paul B. Hoeber, Inc. $6.

It is difficult to recognize the need for a book such as Willis W. Lasher's *Industrial Surgery*. The surgery of trauma can be differentiated from the surgery of disease; but it is after all surgery, governed by the same fundamental principles of anatomy, physiology, and pathology. Industrial surgery, so-called, is surgery, largely traumatic, applied to groups of workmen. Except for entirely extrinsic factors, such as pre-employment examination and compensation, it is no different from surgery applied to any other group. There is perhaps a place for a text, written from the point of view of the experienced physician, on the medico-legal aspects of surgery under compensation conditions. Any attempt to present surgical disease seen in industrial practice—and this book represents such an attempt—must necessarily, to be of value, be exhaustive both from the fundamental and the practical points of view. It must, in fact, be a complete and authoritative monograph on the surgery of trauma.

Unfortunately the present volume fulfils this requirement neither in completeness nor in authority. Furthermore, its arrangement and presentation are confusing and often obscure. Although a section on surgical pathology occurs, there is no reference to the healing processes in wounds of the soft parts. The treatment of this commonest of industrial accidents is accorded six lines for the entire subject of débridement, hidden away under a subsection entitled "Antiseptics." Burns are discussed only under the heading of "Injuries of the Face,

Including Nose, Eyes, and Ears.'' Three pages are given without adequate reference to the profound systemic effects of these injuries. The toxin theory is accepted without reservation. There is no mention of shock or blood concentration and there are no recommendations for their treatment. Carron oil is accepted as the preferable medium for immediate application to the burned area.

These are examples only. The discussion of almost any subject chosen at random will be found to be incomplete, with evidence of confusion in fundamental ideas and with an intensely personal point of view. The phrases ''in our opinion,'' ''we believe,'' and the like occur on almost every page. Ludicrous mistakes are found; such as, ''Creatine is a substance which makes up the ectoderm of arthropods and is almost identical with cartilage.'' The use of the same case material is in at least one instance exactly duplicated without reason (pages 47 and 322). The wrinkling of adhesive plaster strapping shown to illustrate the treatment of sprain of the ankle would not be permitted on the part of a second-year student. Finally, sentence structure is often so faulty as to obscure the meaning, and actual solecisms are frequent. One example may be cited: ''Lacerations of the scalp should be drained [sic] with a small rubber band. They migrate rapidly, producing large pockets of pus. . . .''

Surgeons occasionally encountering industrial injuries may find useful the brief summaries of compensation equivalents in New York State, which appear at the ends of the chapters.

Essentials of Pathology. By Lawrence W. Smith and Edwin S. Gault. Fabrikoid. Pp. 850, with 679 illustrations, New York, N. Y., 1938, D. Appleton-Century Company, Inc. $9.

The authors have written a new type of textbook in which the case-history method of teaching is employed extensively. Most of the illustrations are accompanied by a full clinical history of the corresponding case. The large size of the book is due partly to the inclusion of 295 case reports. These have definite value in most instances, but they are often packed with irrelevant and tedious details. For example, fatty metamorphosis of the liver is illustrated not by a case of chronic alcoholism but by one of primary hypertension. A long story of a mixed tumor of the parotid gland illustrates mucoid degeneration. It would be advantageous to condense the case histories, especially in the sections dealing with general pathology. The teacher who uses this book, of course, must prepare separate case histories to correspond with his own teaching material.

The text is profusely illustrated. There are 679 figures on 160 large plates and 11 of the plates are in color. Most of the illustrations are good, but there are many poor photomicrographs. Because of the space required for case histories and illustrations, the text has been compressed unduly. The discussions are in many instances vague and evasive and betray a lack of wide reading and experience. For example there is a very sketchy discussion of edema on page 46 and on page 415 it is stated the incidence of coronary disease is many times greater in those subject to mental strain than in the phlegmatic.

There are good chapters on the avitaminoses, yaws, and animal parasites.

There are no references to the literature, the authors maintaining that very few medical students ever look up a reference. Medical students may not object to this innovation but the teachers of pathology probably will not take it kindly.

Notwithstanding the weaknesses which have been indicated this book is on the whole of much value. The generous illustrations make it particularly useful to the beginner and some teachers may like the case-history type of presentation.

Clinical Roentgenology of the Digestive Tract. By Maurice Feldman. Cloth. Pp. 1014, with 357 illustrations. Baltimore, 1938, William Wood and Company. $10.

This unusual monograph will fill a long felt need by clinicians. Within its pages the author recounts the clinical and roentgenologic aspects of all diseases of the digestive tract and its appendages. The number of rare diseases concerning which information is made available in this text is astounding. Intussusception of the jejunum into the stomach through the stoma after gastroenterostomy, hypertrophy of the pylorus of the adult, and other rare occurrences are given thoughtful consideration. It is somewhat surprising to note that the author omitted mention of the inverted position in detection of the site of occlusion in imperforation of the anal canal and rectum, a helpful roentgen finding.

The author's object in writing the book was "to bring together sources of material which have not heretofore been compiled in a single volume." Surgeons, internists, and roentgenologists owe a debt of gratitude to the author for this worthwhile accomplishment. It should prove an extremely valuable source book.

A Manual of Surgery for Nurses. By Charles Wells. Pp. 490, with 160 illustrations. Baltimore, 1938. William Wood and Company. $4.

This manual covers a very difficult field in a satisfactory manner. The author evidently realizes the inadequacy of the general preliminary training of the nurse and the difficulties thus encountered in her understanding of the problems of surgery. He takes nothing for granted and thus is able to describe the general field of surgery in a very simple and unostentatious manner. This method of attack does lend itself to some criticism, however, in that in many instances the subjects are dismissed with too little attention. In spite of this brevity, the vital points of the subject are covered and undoubtedly adequately enough so that they will remain fairly distinct entities in the nurse's mind, which might not be the case if the text were lengthy.

A favorable aspect of this work is that, although it is primarily intended to give a nurse some conception of surgical conditions, in each instance where nursing care is of paramount importance, the author has designated what the special duties of the nurse shall be.

Included in the text are 159 pen-line, black and white drawings, besides a frontispiece showing the thoracic and abdominal viscera.

The text includes the surgical specialties of urology, gynecology, and orthopedics, as well as eye, ear, nose, and throat.

The chapters are divided on a regional basis and include all of the more common, important diseases. The rare diseases fortunately are not mentioned.

The discussion of each disease is limited mainly to a description of the pathology of the disease and treatment. The diagnoses and differential diagnoses are not emphasized, as they are not in the province of the nurse and would only serve to confuse her.

This book is recommended for those nurses who are taking a preliminary course in surgery. It will give them an excellent understanding of the basic problems of surgery. For those doing postgraduate work and for those who are specializing in surgical nursing, it should be supplemented by other reading.

Digestive Tract Pain. By Chester M. Jones. Cloth. Pp. 152, with 5 illustrations, New York, 1938, The Macmillan Company. $2.50.

In this small monograph the author relates a summary of observations dating back over a period of fourteen years, during which time he has been investigating digestive tract pain. The technique involved concerned the swallowing of a small inflatable rubber balloon attached to a fine rubber tube by the subject under investigation. The position of the tube was checked by fluoroscopy. Overdistending a short segment of the alimentary tract induced spasm and caused pain. In his observations on pain in the pelvic colon and rectum, the author observed that twelve feet of tube on the average sufficed to permit the tube to reach from mouth to rectum.

The author investigated the production of pain in the esophagus, stomach, duodenum, ileum, and jejunum, as well as the various segments of the colon. Scatterograms are employed to indicate the location of the distress produced. Selected case histories occupy about one-half of the text. A concluding chapter on therapeutic considerations relates briefly the author's attitude toward the management of various types of abdominal ills. A few well-chosen references are appended.

This small text will be read with engaging concern by all interested in digestive tract pain, a fairly common denominator of diseases of the alimentary canal. Whereas the scatterograms indicate a certain constancy in the sites at which spasm of a segment of the digestive tract provokes pain (a feature particularly notable in the cecum), yet the clinician will find little encouragement that abdominal pain presented by a patient may now be interpreted with greater ease or more precision. However, he who reads this text with the care and attention that it merits will acquire a better understanding of the mechanism of digestive tract pain.

Surface and Radiological Anatomy. By Arthur B. Appleton, William J. Hamilton, and Ivan C. C. Tchaperoff. 338 illustrations. Baltimore, 1938, William Wood & Company.

There is an increasing tendency in the modern teaching of anatomy to devote considerable time to practical application. That the study of normal, living anatomy can be best made through the medium of roentgenology is well understood. It is curious, therefore, that so little time is devoted to this phase of anatomy in many medical schools and that no text devoted exclusively to this study has heretofore been published. The volume under consideration combines a study of surface anatomy, clinical applications, and roentgen anatomy. At first thought there seems little connection between the first subject and the third, but the correlation of these two is due to the fact that both are a part of any system of clinical anatomy. The authors present in brief form the principal anatomical features of the body surface with adequate explanations of their significance and relationship to underlying structures. They correlate these with clinical methods of examination, such as percussion, bronchoscopy, and so forth. In addition they

describe briefly, but adequately, the normal roentgen appearance of the same anatomical parts, including the skeleton and those viscera which can be demonstrated by this method.

The subject of normal roentgen anatomy, if treated in reasonable detail, especially if normal variations are included, would be sufficient in itself to justify a good-sized text. The authors have been sufficiently concise and sufficiently gross in their general treatment so that the work is well balanced. The illustrations are numerous and well reproduced. The roentgenograms are clear, for the most part well labeled, and are often accompanied by correlating anatomical diagrams. A few anatomical variations are presented, such as the azygos lobe of the lung, although the far more common inferior accessory lobe is omitted. The development of the skeleton is presented by roentgenograms and a table of ossification centers is included in the appendix. The latter is sufficiently accurate for clinical purposes, but it should be noted that the epiphysis for the tuberosity of the fifth metatarsal is not given.

The correctness of the position of the left atrium on the roentgenograms of the heart is open to question. An elaboration of the description of the bronchial tree and of the significance of the linear markings of the lungs would be of value. In general, however, there is little to criticize other than the brevity of the work, which is, at the same time, a virtue.

This book may not be fully suitable as an applied anatomy for surgeons nor is it sufficiently detailed to completely serve as a normal roentgen anatomy for radiologists. For the student of anatomy, for the practicing physician, and for the beginning student of radiology, this volume will be instructive and of great practical value. It is a most valuable accessory to the usual text on gross anatomy.

Essentials of Obstetrical and Gynecological Pathology With Clinical Correlation. By Marion Douglas and Robert L. Faulkner. Pp. 187, with 148 illustrations. St. Louis, 1938, The C. V. Mosby Company. $4.75.

This volume is primarily designed to be of value in teaching the essentials of gynecological and obstetrical pathology to medical students and resident staffs of hospitals, as well as to men who have been engaged in active practice and who have not had the opportunity to study even a minimal amount of pathology.

In 155 pages, in which are included 126 illustrations and smatterings of symptomatology and treatment, the authors endeavor to present the essentials of gynecological pathology. In the remainder of the volume, 21 pages, containing 42 illustrations, the essentials of obstetrical pathology are presented. Though arranged in excellent sequence and though the photomicrographs are excellent with very explanatory notes, the reviewer believes that this volume falls far short of presenting material that he would consider as essentials of gynecological and obstetrical pathology. The material, though well presented, is too sketchy and is not complete enough even to fall under the caption of essentials. There is no bibliography.